Comparison between the efficacy of Ultrasound Guided Continous Intercostal Nerve Block and Ultrasound Guided Continous Thoracic Paravertebral Block in management of Post-Thoracotomy pain by using Bupivacaine versus Bupivacaine and Dexmedetomidine

Thesis

Submitted For Fulfilment of the MD Degree in Anesthesia and Intensive Care

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دراسة مقارنة بين فعالية الحقن المستمر بين الضلوع والحقن المستمر بجانب الفقرات الصدرية باستخدام الموجات فوق الصوتية فى تسكين الألم بعد عمليات الشق الصدرى باستخدام عقار البيوبيفاكين ضد عقار البيوبيفاكين المضاف اليه عقار الديكسميديتوميدين

توطئة للحصول على درجة الدكتوراة فى التخدير والعناية المركزة

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2018

بسم الله الرحمن الرحيم

وقل اعملوا

فسيرى الله عملكم

ورسوله والمؤمنون

صدق الله العظيم

سورة التوبة آية ١٠٥

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List of Abbreviations

ABG	Arterial blood gases
APS	American pain society
ASA	American society of anesthesiology
BIS	Bispectral index
BMI	Body mass index
BPF	Bronchopleural fistula
CGRP	Calcitonin gene-related peptide
CNS	Central nervous system
COPD	Chronic obstructive pulmonary disease
COX-2	Cyclo-oxygenase-2
CSF	Cerebrospinal fluid
CT	Computed tomography
CVP	Central venous pressure
DLT	Double lumen tube
ECG	Electrocardiogram
ETT	Endotracheal tube
FLACC	Face, Legs, Activity, Cry, Consolability scale
FEV1	Forced expiratory volume 1
FRC	Functional residual capacity
FVC	Forced vital capacity
G I	Gasterointestinal
GABA	Gaba amino butyric acid
HR	Heart rate
ICNB	Intercostal nerve block
ICNs	Intercostal nerves
ICSs	Intercostal spaces
ICU	Intensive care unit
IV	Intravenous
LA	Local anesthetic
MAP	Mean arterial pressure
MEC	Minimal effective concentration
MHz	Mega hertz
MPQ	McGill pain Questionaire
NSAIDs	Non steroidal anti-inflammmatory drugs
OLV	One lung ventilation
PACU	Postoperative anesthesia care unit
PAG	Periaqueductal grey
PAOP	Pulmonary artery oxygen pressure

PCA	Patient controlled anesthesia
PE	Pulmonary embolism
PRA	Pain rescue analgesia
PTPS	Post-thoracotomy pain syndrome
PVB	Paravertebral block
RBCs	Red blood cells
RR	Respiratory rate
SP	Substance P
TAP	Transversusabdominis plane
TENS	Transcutaneous electrical nerve stimulation
TNS	Transient neurologic symptoms
TPVs	Thoracic paravertebral space
VAN	Vein, artery, nerve
VAS	Visual analogue score
α2-AR	Alpha 2 adrenergic receptors

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Acknowledgment

First and foremost, thanks to **(ALLAH),** the Most Gracious and the Most Merciful, who granted me to finish this work.

Prayer and peace be upon the most honorable of Messengers **(MOHAMAD).**

I wish to express my thanks & respects to: ***Prof. Ehab Ahmed Abd El Rahman*** Professor of Anesthesia and ICU department, Benha Faculty of medicine, Benha University, for his constructive and instructive comments, valuable suggestions and continuous support.

Also, I send my deepest gratitude and appreciation to ***Dr. Ehab Saeed Abd El Azeem*** Assistant professor of Anesthesia and ICU department, Benha Faculty of medicine, Benha university, for his precious efforts and his helpful advices as well as his continuous monitoring of the work and support of the study.

I wish to express my deep gratitude and profound appreciation to ***Dr. Ahmed Abd El Hmid Hassan*** Lecturer of Anesthesia and ICU, Faculty of Medicine, Benha University for his close supervision, generous assistance and valuable support throughout this work.

Last but not least, I also would like to thank my Family, close friends, my helpful collogues and every patient included in our study.

Salsabil Sayed Abd El Kader

Introduction

Patients undergoing thoracic surgery are usually high-risk patients. They are most often elderly, have concurrent medical co-morbidities and have poor physical status either due to the malignancy, malnutrition and the pre-existing primary disease. Most of these patients are smokers, have occupational exposure and are therefore at even greater risk of developing pulmonary complications. Part of their problem is due to their poor baseline pulmonary function. Pulmonary complications may manifest in the operating room itself or in the post-anesthesia care unit (PACU), intensive care unit (ICU) and also in the surgical ward. Thoracic surgeries are usually of longer duration; they frequently have significant blood loss and fluid shifts. The surgeries as well as the anesthetic techniques run the risk of damaging intrathoracic structures such as the lungs, airways and the peripheral nervous systems. Both general anesthesia and thoracic surgery produce changes in the respiratory system. Together with underlying conditions, they can be responsible for post-operative pulmonary complications **(Rock and Rich, 2003).**

Post-thoracotomy pain syndrome is defined by the International Association for the Study of Pain as pain that recurs or persists along a thoracotomy incision at least two months following the surgical procedure. In general, it is burning and stabbing pain with dysesthesia and thus shares many features of neuropathic pain **(Koehler and Keenan, 2006).**

There are different analgesic modalities for management of post-thoracotomy pain. There are systemic methods which includes infusion and patient-controlled analgesia (PCA) or regional techniques that mainly rely on epidural, intrathecal or paravertebral blocks. Other techniques

range from intercostal nerve block to cryoprobeneurolysis **(Slinger, 2004).**

Intercostal nerve blockade is used routinely at some centers either by single injection of local anesthetics in multiple intercostal nerves before closure of thoracotomy incision or catheter infusion. However, single-shot intercostal nerve blocks with local anesthetic generally do not provide effective long-term analgesia and frequently have to be repeated **(Luketich et al, 2005).**

The thoracic paravertebral block is another technique for management of post-thoracotomy pain by injecting local anesthetic in the vicinity of the thoracic spinal nerves emerging from the intervertebral foramen with the resultant ipsilateral somatic and sympathetic nerve blockade. The resultant anesthesia or analgesia is conceptually similar to a "unilateral" epidural anesthesia **(Vogt et al, 2005).**

The addition of adjunctive analgesics, such as fentanyl and clonidine, to local anesthetics has been shown to enhance the quality and duration of sensory neural blockades, and decrease the dose of local anesthetic and supplemental analgesia **(Mohamed et al, 2014).**

Dexmedetomidine is a highly selective α2-adrenorceptor agonist recently introduced to anesthesia; it produces a dose-dependent sedation, anxiolysis, and analgesia (involving spinal and supraspinal sites) without respiratory depression **(Khan et al, 1999).**

Aim of the work

This prospective randomized double blinded clinical study will be done to evaluate efficacy of both ultrasound guided continuous intercostal and ultrasound guided continuous paravertebral block on thoracotomy pain and their benefit on reducing pulmonary complications and its efficacy in reducing amount of narcotics and which one is better.

Anatomy of intercostal space:

Intercostal spaces:

The spaces between the ribs are called intercostal spaces. Each space contains three muscles of respiration: the external intercostal, the internal intercostal, and the transversus thoracis muscle. The transversus thoracis muscle is lined internally by the endothoracic fascia, which is lined internally by the parietal pleura. The intercostal nerves and blood vessels run between the intermediate and deepest layer of muscles. They are arranged in the following order from above downward: intercostal vein, intercostal artery, and intercostal nerve (i.e., VAN) **(Snell, 2012).**

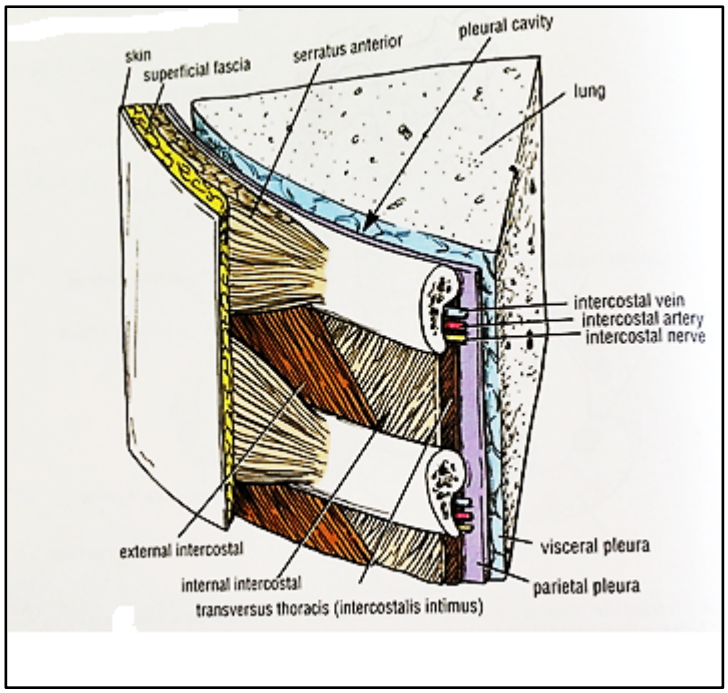

Fig. (1): Section through an intercostal space **(Snell, 2012)**

Muscles:

Intrinsic Chest Wall Muscles:

The intercostal muscles are thin multiple layers of muscular and tendinous fibers that occupy the intercostal spaces; their names are derived from their spatial relationship, i.e. the external, internal and innermost intercostals**. (Drake, 2005)**

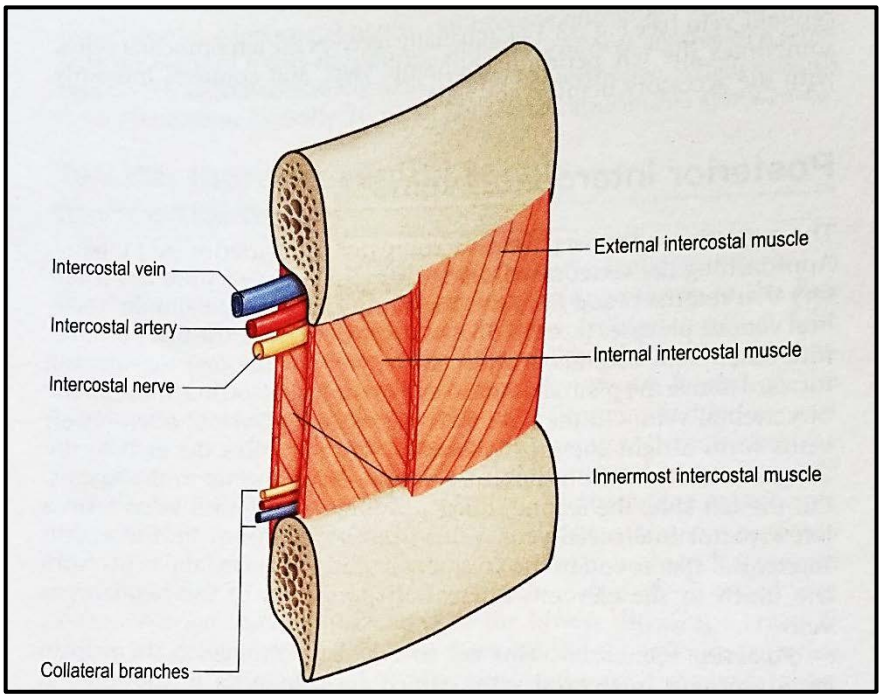

Fig. (2): Dissection of part of an intercostal space, showing the position of the intercostal vessels and nerves relative to intercostal muscles **(Gross, 1996).**

The intercostal nerves:

The intercostal and subcostal nerves are the ventral rami of the twelve thoracic spinal nerves. Typically these nerves run forward in an intercostal space deep to the internal intercostal membrane and muscle and below the intercostal vessels. They give off a lateral cutaneous branch that pierces the intercostal and superficial muscles to reach and supply the skin of the lateral thoracic wall, and collateral branch that runs

forward along the lower border of the space. At the lateral border of the sternum nerves pass anteriorly and terminates as anterior cutaneous branches. Along their course they supply the intercostal muscles. An intercostal nerve follows closely the distribution of the ventral ramus of a typical segmental nerve **(Gross, 1996).**

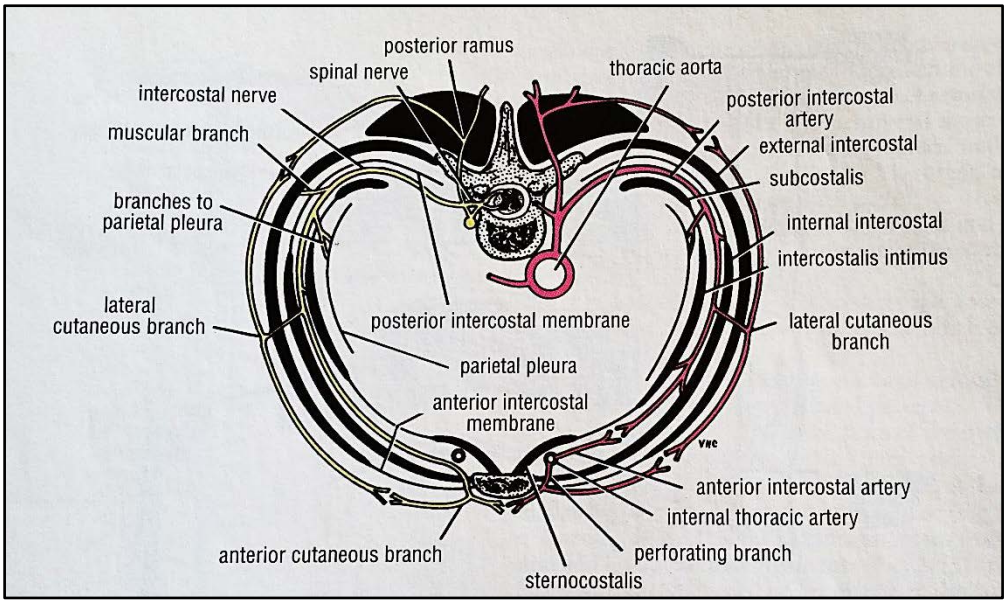

Fig. (3) Cross section of thorax, showing distribution of a typical intercostal nerve and posterior and anterior intercostal artery **(Snell , 2012).**

Sonoanatomy:

In the majority of cases, it is not possible to visualize sonographically the ICNs in the ICSs lateral to costal angles. In this region, the ICNs are very close to the rib thus visibility is impeded by bone shadow. Also, the nerves are progressively smaller when course beyond the costal angles. The intercostal muscles, ribs and pleura are important landmarks that are easily recognized leading to the intercostal nerves **(Narouze, et al., 2012).**

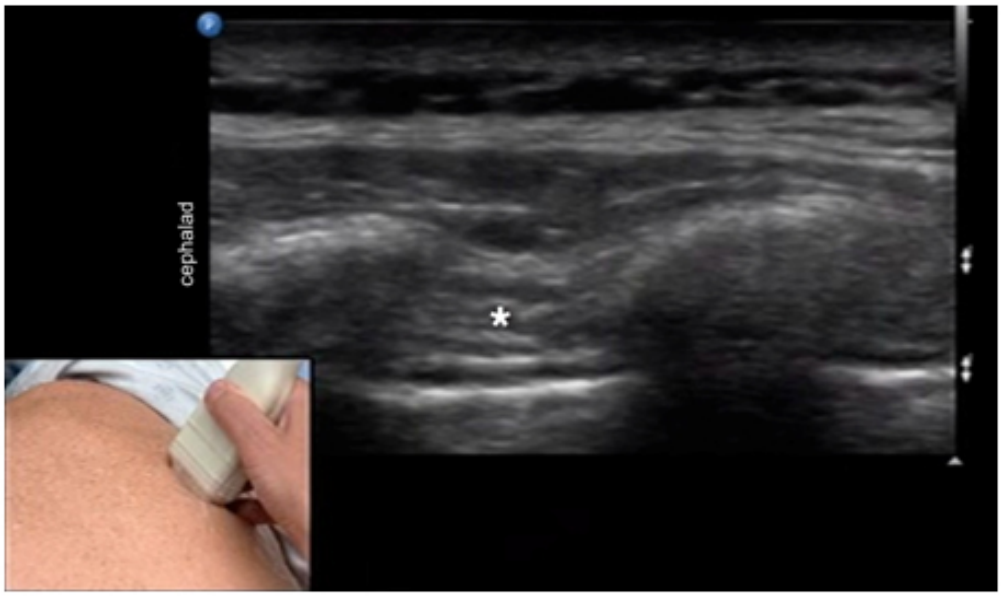

Fig. (4) Sonogram showing the intercostal space lateral to the costal angle denotes fascial layer between the external and internal intercostal muscles; the intercostal nerve is not visualized in this region **(Patel and Joshi, 2013).**

Anatomy of thoracic paravertebral space:

The thoracic paravertebral space (TPVS) is a wedge-shaped space that lies on either side of the vertebral column .It is wider on the left than on the right **(Maclntosh and Bryce-Smith 1962; kittredge, 1983).**

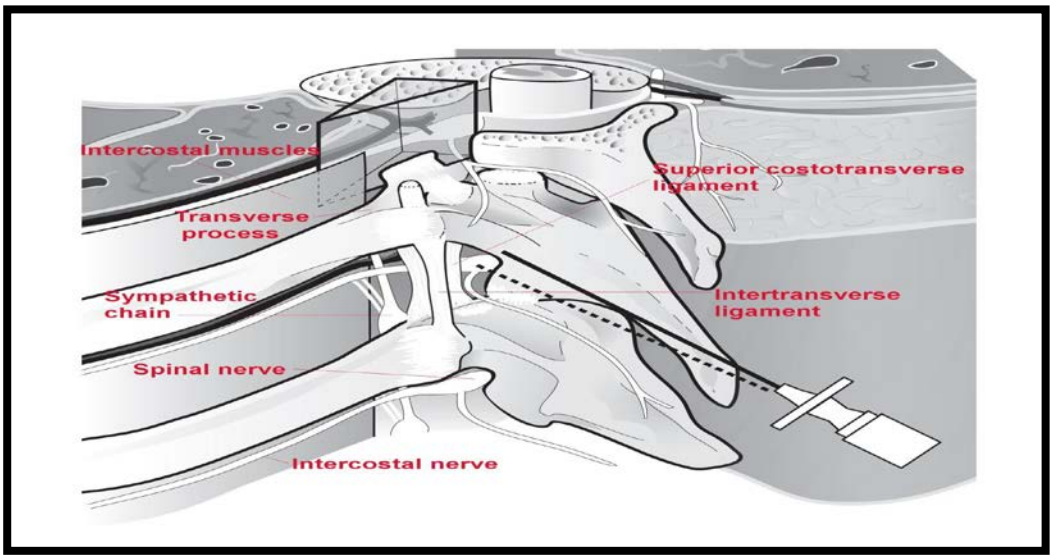

Fig. (5): Drawing of the thoracic paravertebral space **(Mark and John, 2011).**

The parietal pleura forms the anterolateral boundary, while the base is formed by the posterolateral aspect of the vertebral body, the intervertebral disc, the intervertebral foramen and its contents **(Eason and Wyatt, 1979; Maclntosh and Bryce-Smith, 1962).**

The superior costotransverse ligament, which extends from the lower border of the transverse process above to the upper border of the transverse process below, forms the posterior wall of the TPVS. The apex of the space is continuous, with the intercostal space lateral to the tips of the transverse processes **(Eason and Wyatt 1979; Maclntosh and Bryce-Smith, 1962).**

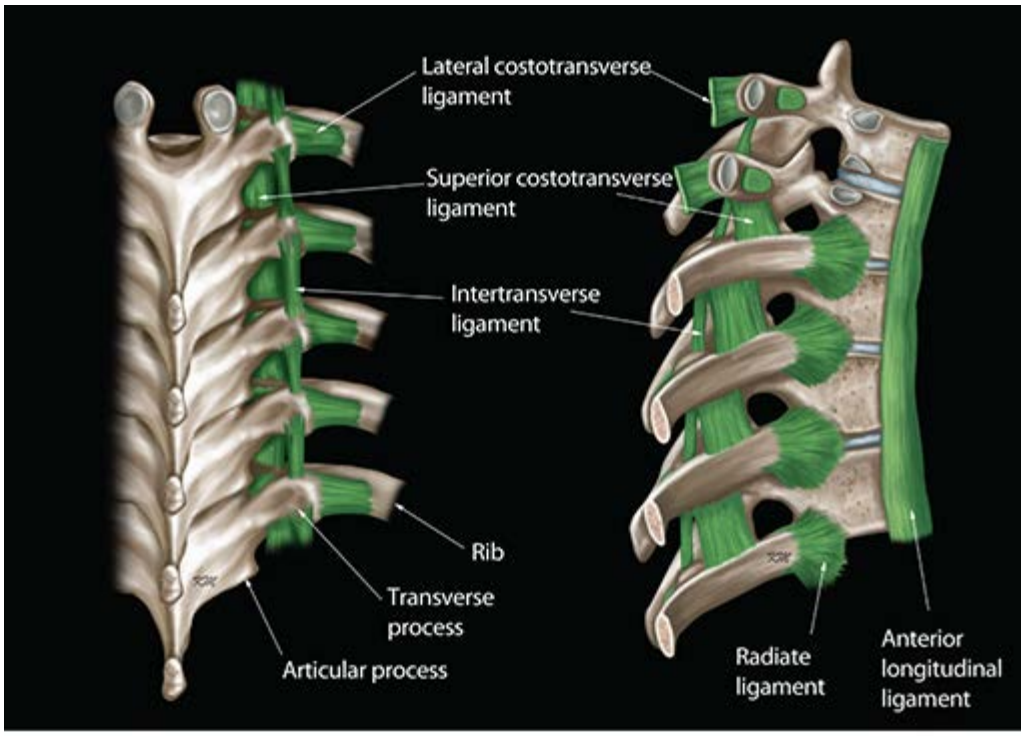

Fig. (6) Paravertebral ligaments relevant for thoracic paravertebral block **(Manoj et al., 2017).**

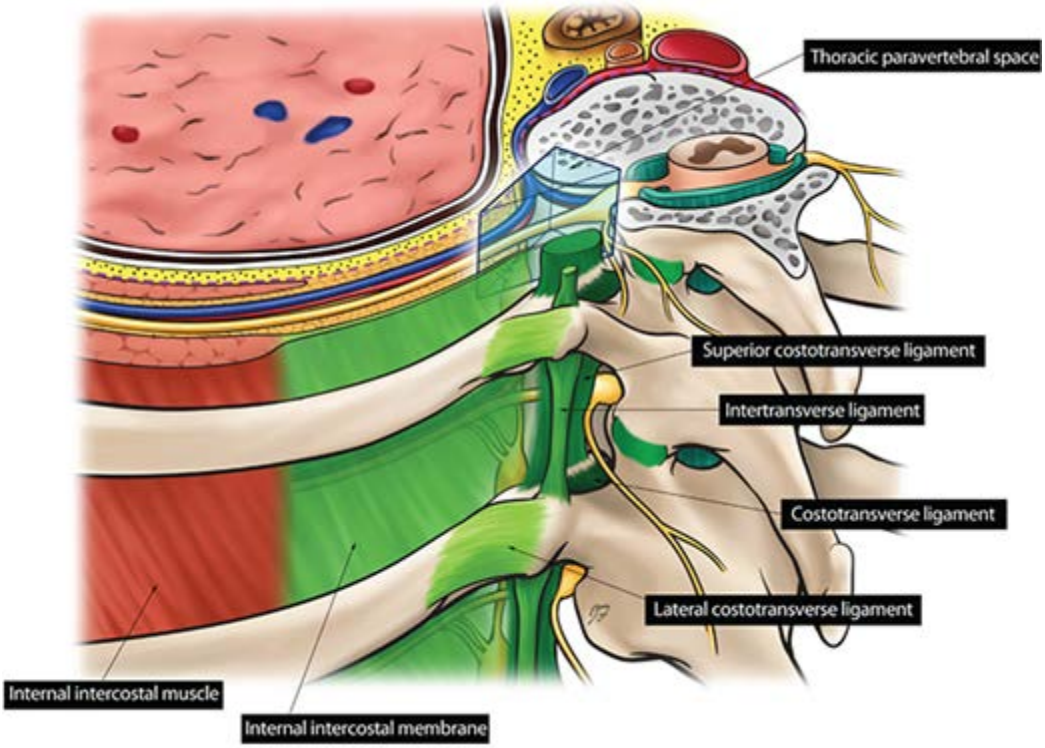

Fig. (7) Anatomy of the thoracic paravertebral region showing the various paravertebral ligaments and their anatomical relationship to the thoracic paravertebral space **(Manoj et al., 2017)**.

Interposed between the parietal pleura and the superior costotransverse ligament is a fiberoelastic structure, the endothoracic fascia, which is the deep fascia of the thorax and lines the inside of the thoracic cage **(Tenicela and Pollan, 1990; Dugan and Samson, 1975).**

In the paravertebral location, the endothoracic fascia is closely applied to the ribs and fuses medially with the periosteum at the midpoint of the vertebral body **(Maclntosh and Bryce-Smith, 1962; Moore, et al, 1980).**

The spinal nerves in the TPVS are segmented into small bundles lying freely among the fat and devoid of a fascial sheath, which makes them exceptionally susceptible to local anesthetic block **(Nunn and Salvin, 1980).**

The intercostal nerve and vessels are located behind the endothoracic fascia, while the sympathetic trunk is located anterior to it in the TPVS **(Moore, 1981)**.

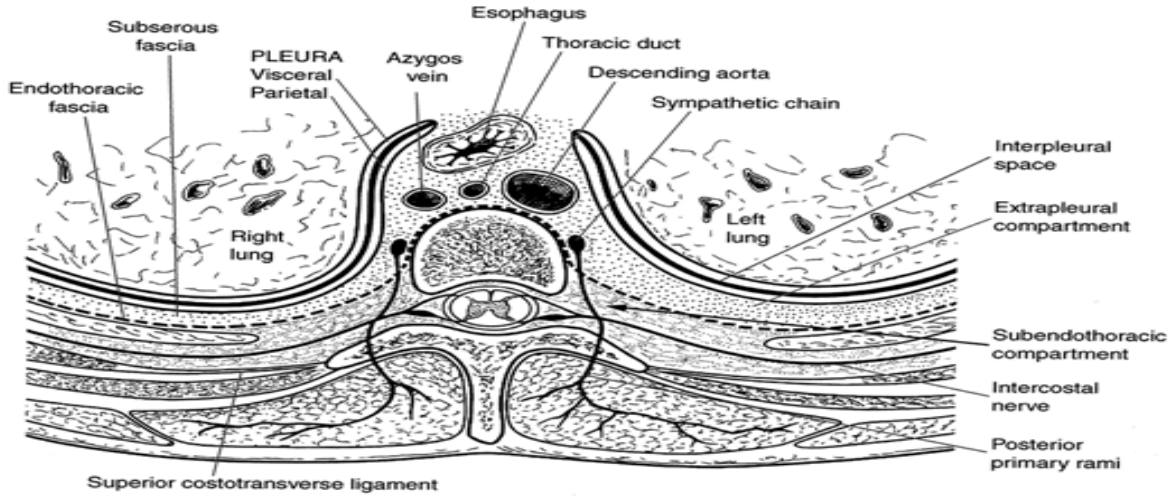

Fig. (8). Anatomy of the thoracic paravertebral space **(Manoj et al., 2017)**.

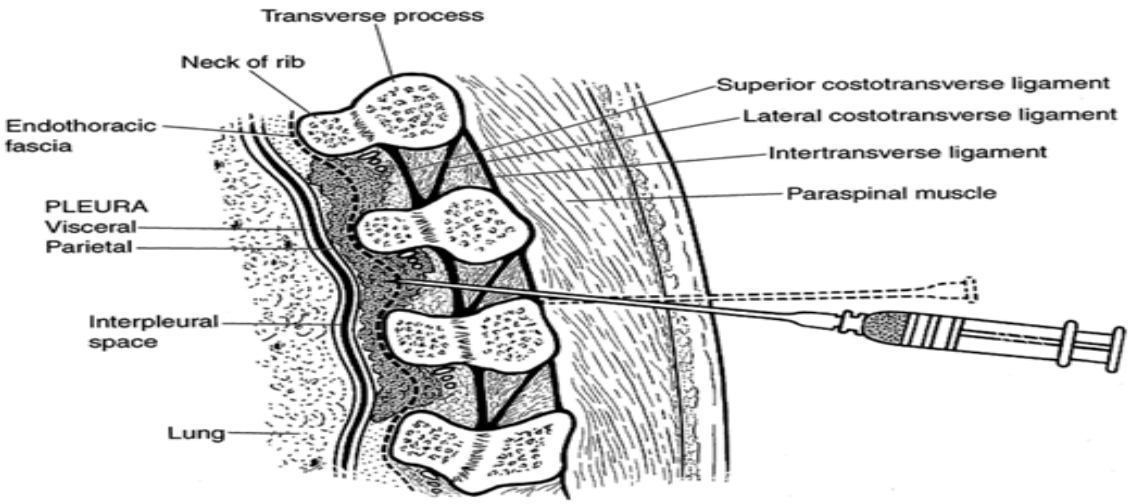

Fig. (9) Saggital section through the thoracic paravertebral space showing a needle that has been advanced above the transverse process **(Manoj et al., 2017)**.

Sonoanatomy

Usually start imaging with a high-frequency linear probe and change to a low-frequency curvilinear probe if imaging is difficult. The curved probe provides a wider field of view which can help identify the midline and pleura during transverse scanning but at lower resolution. The transverse process projects posteriorly, and the costotransverse articulation is on its anterior aspect, forming a step in bony depth and angle to allow identification of the transverse process tip with ultrasound. With a transverse probe orientation, the acoustic shadow of these bony margins becomes deeper at the point where the transverse process joins the rib. It is important to distinguish the pleura from the acoustic shadow of bone – pleura moves with inspiration, and some penetration of ultrasound occurs. The pleura can be distinguished from bone more easily in the sagittal plane – it is the deeper hyperechoic structure. Local anesthetic injected into the paravertebral space should increase the depth between transverse process and parietal pleura. Identification of the radicular vessels using color flow Doppler while scanning the paravertebral space is difficult because of the depth

and size of the vessels, and the presence of acoustic shadow (**Lonnqvist and Hesser, 1993).**

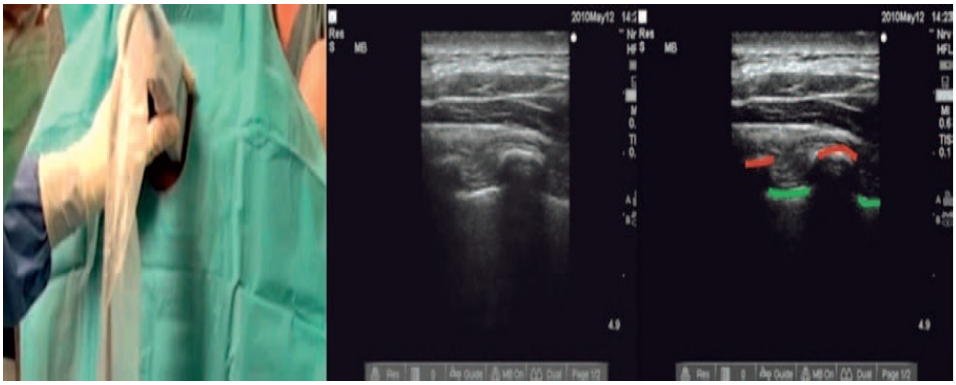

Figure (10): Sonoanatomy of paravertebral space, US probe in sagittal paramedian plane; Red line-transverse process, Green line-parietal pleura **(Attila et al., 2010)**.

Pain physiology, assessment and management

Classification of pain

Pain can be categorized according to several variables, including its duration (acute or chronic), its pathophysiologic mechanisms (nociceptive or neuropathic), and its clinical context (e.g., postsurgical, malignancy related, neuropathic, degenerative). Acute pain follows traumatic tissue injuries, is generally limited in duration, and is associated with temporal reductions in intensity. Chronic pain may be defined as discomfort persisting 3–6 months beyond the expected period of healing. In some chronic pain conditions, symptomatology, underlying disease states, and other factors may be of greater clinical importance than definitions based on duration of discomfort **(Vadivelu et al., 2009).**

Somatic pain can be further classified as superficial or deep. Superficial somatic pain is due to 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. Deep somatic pain arises from muscles, tendons, joints, or bones **(Kaikman et al 2007).**

The visceral form of acute pain is 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 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 to the area around the organ or referred to a distant site (Table 1). The phenomenon of visceral or parietal pain referred to cutaneous areas results from patterns of embryological development and migration of tissues, and the convergence of visceral and somatic afferent input into the central nervous system. Thus, pain associated with disease processes involving the peritoneum or pleura over the central diaphragm is frequently referred to the neck and shoulder, whereas disease affecting the parietal surfaces of the peripheral diaphragm is referred to the chest or upper abdominal wall **(Ready & Edwards 2006).**

Table (1): Patterns of Referred Pain:

Location	Cutaneous Dermatome
Central diaphragm	C4
Lungs	T2–T6
Heart	T1–T4
Aorta	T1–L2
Esophagus	T3–T8
Pancreas and spleen	T5–T10
Stomach, liver, and gallbladder	T6–T9
Adrenals	T8–L1
Small intestine	T9–T11
Colon	T10–L1
Kidney, ovaries, and testes	T10–L1
Ureters	T10–T12
Uterus	T11–L2
Bladder and prostate	S2–S4
Urethra and rectum	**S2–S4**

(Ready & Edwards 2006).

Pain pathway:

Nociception is a sequential process that includes transduction of noxious stimuli into electrical signals by peripheral nociceptors, conduction of encoded signals by afferent neurons to the dorsal horn of the spinal cord, and subsequent transmission and modulation of the signals at both spinal and supraspinal levels. In its simplest form, the nociceptive pathway is a three neuron chain. (figure 11)The 1st neuron in the chain the primary afferent neuron is responsible for transduction of noxious stimuli and conduction of signals from the peripheral tissues to neurons in the dorsal horn of the spinal cord **(Lemke et al., 2004)**.

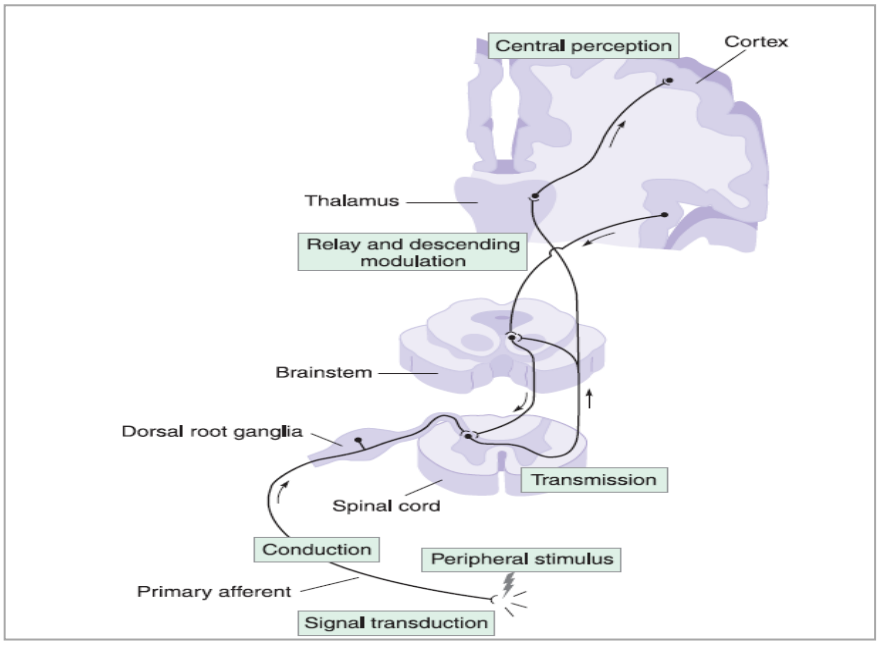

Fig. (11): Nociceptive pathway **(Lemke et al., 2004)**

Nociceptive fibers synapse with 2nd order nociceptive neurons in the dorsal horn of the spinal cord. There are 2 main types of nociceptive neurons in the dorsal horn (projection neurons and interneurons), and these neurons are organized into layers or laminae. Neurons that mediate

nociception are located primarily in lamina I (substantiagelatinosa), lamina II (marginal layer), and lamina V. Projection neurons are located in laminae I and V and have axons that "project" to supraspinal 3rd-order neurons. Neurons located primarily in lamina I receive input directly from nociceptive Aδ and C fibers and are called nociceptive-specific neurons **(Lemke et al., 2004).**

The 2nd neuron in the chain - the projection neuron - receives input from the primary afferent neurons and projects to neurons in the medulla, pons, midbrain, thalamus, and hypothalamus.Ascending nociceptive tracts, including the spinothalamic, spinobulbar, and spinohypothalamic tracts, convey nociceptive information from the dorsal horn of the spinal cord to higher centers in the central nervous system. The spinothalamic pathway is the major ascending nociceptive pathway; it is divided into medial and lateral components. The medial component projects to medial thalamic nuclei and then (via 3rd-order neurons) to the limbic system; it is responsible for transmission of nociceptive input involved with the affective-motivational aspect of pain. The lateral component projects to lateral thalamic nuclei and then to the somatosensory cortex; it is responsible for transmission of nociceptive input involved with the sensory-discriminative aspect of pain. The 3rd order, supraspinal neurons integrate signals from the spinal neurons and project to the subcortical and cortical areas where pain is finally perceived **(Lemke et al., 2004)**.

Chemical Mediators of Pain:

Neurotransmitters are chemicals that allow the movement of information from one neuron across the gap between it and the adjacent neuron. The release of neurotransmitters from one area of a neuron and the recognition of the chemicals by a receptor site on the adjacent neuron

causes an electrical reaction that facilitates the release of the neurotransmitter and its movement across the gap **(Thomas et al., 2005).**

Several neuropeptides and excitatory amino acids function as neurotransmitters for afferent neurons subserving pain (Table 2). Many if not most neurons contain more than one neurotransmitter, which is simultaneously coreleased. The most important of these peptides are substance P (sP) and calcitonin gene-related peptide (CGRP). Glutamate is the most important excitatory amino acid**(Dawes et al., 2013).**

Table (2): Major Neurotransmitters Mediating or Modulating Pain.

Neurotransmitter	**Receptor**	**Effect on Nociception**
Substance P	NK–1	Excitatory
Calcitonin gene-related peptide		Excitatory
Glutamate	NMDA, AMPA, kainite, quisqualate	Excitatory
Aspartate	NMDA, AMPA, kainite, quisqualate	Excitatory
Adenosine triphosphate (ATP)	P_1, P_2	Excitatory
Somatostatin		Inhibitory
Acetylcholine	Muscarinic	Inhibitory
Enkephalins		Inhibitory
-Endorphin		Inhibitory
Norepinephrine		Inhibitory
Adenosine	A_1	Inhibitory
Serotonin	5-HT_1 (5-HT_3)	Inhibitory
-Aminobutyric acid (GABA)	A, B	Inhibitory
Glycine		Inhibitory

(Dawes et al., 2013)

As important as the ascending pathways are fibers that descend from brainstem to spinal cord to modulate the incoming signals. Notable neurotransmitters mediating this anti-nociceptive effect include nor adrenaline (nor epinephrine), especially in the locus coeruleus, and serotonin in the raphe nuclei. Opioid receptors are prevalent here. Some descending connections are:

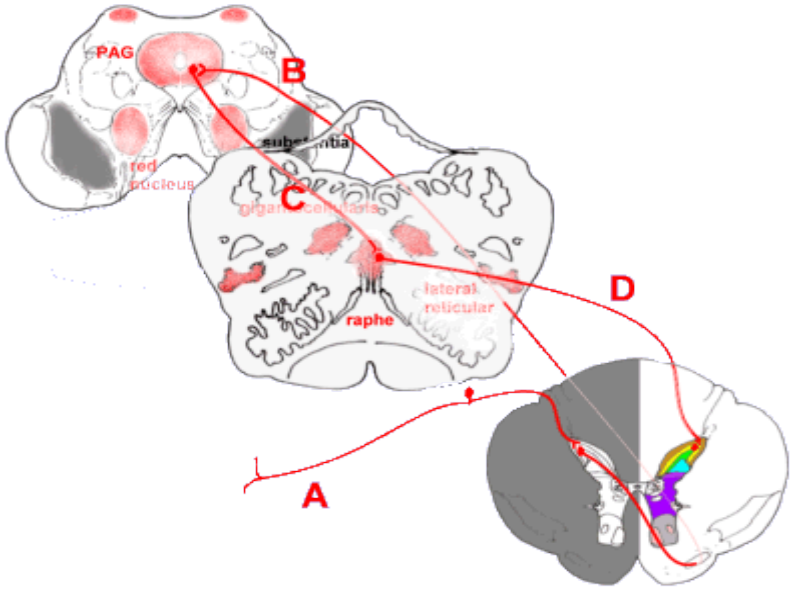

Fig. (12) Descending connections that modulate incoming pain impulses **(Sutin& Carpenter 2004).**

Incoming painful stimuli are transmitted (A) to the dorsal horn, and from there (B) to the periaqueductal grey (PAG). Descending impulses pass (C) to the raphe nuclei, especially the nucleus raphe magnus, in the upper medulla, and thence back to the dorsal horn via reticulospinal fibers (D). The above shows only the serotonergic descending fibers. Other pain-suppressing impulses pass from the PAG to the locus coeruleus, and from there to the dorsal horn **(Sutin& Carpenter, 2004).**

Assessment of Acute Pain

Based on the assumption that patient self-reporting is the "most reliable indicator of the existence and intensity of pain" the ideal tool for pain will identify the presence of pain and its evolution over time. In addition, tools should be applicable to any person regardless of age, race, creed, socioeconomic status, and psychological or emotional background **(Rowbotham& Macintyre, 2003).**

Assessment of pain in adults:

In the assessment of pain intensity, rating scale techniques are often used. The most commonly used forms are:

- The Category Rating Scales: (e.g. none, mild, moderate, severe, unbearable or 1-5).
- The Visual Analogue Scales (VAS): (e.g. 10 cm line with anchor points at each end). The VAS has been shown to be more sensitive to change and is therefore more widely used. These scales may also be incorporated into pain diaries.
- McGill Pain Questionnaire (MPQ): (78 pain adjectives arranged into 20 groups further arranged into sets of words describing sensory aspects of the quality of pain). Very widely used questionnaire**(Svensson et al., 2007).**

A Visual Analogue Scale (VAS) is a measurement instrument that tries to measure a characteristic or attitude that is believed to range across a continuum of values and cannot easily be directly measured**.**

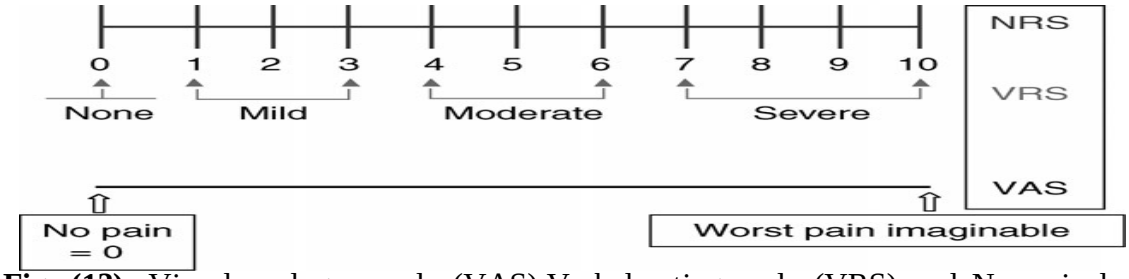

Fig. (13): Visual analogue scale (VAS).Verbal rating scale (VRS) and Numerical rating scale (NRS) **(Breivik et al., 2000).**

Operationally a VAS is usually a horizontal line, 100 mm in length, anchored by word descriptors at each end, as illustrated in (Fig. 13). The patient marks on the line the point that they feel represents their perception of their current state. The VAS score is determined by measuring in millimetres from the left hand end of the line to the point that the patient marks. There are many other ways in which VAS have been presented, including vertical lines and lines with extra descriptors (**Niven&Dowens,2000).**

Assessment of acute pain during movement (dynamic pain):

Assessment of the intensity of acute pain at rest after surgery is important for making the patient comfortable in bed. However, adequate relief of dynamic pain during mobilization, deep breathing, and coughing is more important for reducing risks of cardiopulmonary and thromboembolic complications after surgery. Immobilization is also a known risk factor for chronic hyperalgesic pain after surgery, becoming a significant health problem in about 1%, a bothersome but not negligible problem in another 10%. Effective relief of dynamic pain facilitates mobilization and therefore may improve long-term outcome after surgery **(Jarzyna et al., 2011).**

Multimodal Pain Management

To address the under-treatment of postoperative pain and the limitations of opioid monotherapy, a strategy known as multimodal pain management was introduced in the early 1990s. This approach simultaneously administers two or more analgesic agents with different mechanisms of action. Combination therapy using drugs with distinct mechanisms of action may add analgesia or have a synergistic effect and allow for better analgesia with the use of lower doses of a given medication than if the drug was used alone **(Pasero, 2011)**.

For example, postoperative multimodal analgesia may consist of the use of opioid and non-opioid pharmacologic agents, as well as regional anesthesia and continuous peripheral nerve block. The multimodal approach has been used by many professional organizations, including the American Society of Anesthesiologists (ASA) and the American Pain Society (APS) **(Jarzyna et al., 2011)**.

Ultrasound guidance has greatly influenced the practice of regional anesthesia in the last 15 years. Between 1884, the year when **Carl Koller** performed the first regional block for eye surgery in Vienna, and the late 1970s, the main developments were in new local anesthetic drugs and the introduction of mainly anatomical methods for nerve identification. Unfortunately, anatomy is not exactly predictable and the natural variability of human anatomy led to poor success rates for many peripheral nerve blocks **(Kapral et al., 1994)**.

Current ultrasound equipment allows much easier identification of very small neural structures than it was possible with machines introduced only a few years ago. In addition, adjacent anatomical structures can be identified **(Duggan et al., 2009).**

Without any doubt, direct visualization of neural and adjacent anatomical structures is the main advantage of the use of ultrasound for regional block techniques. An important objective for ultrasound is visualization of the spread of local anesthetic during injection. Confirmation of the correct disposition of local anesthetic avoids any maldistribution , such as epineural, perineural or intravascular injection. In addition, an ability to perform blocks with small volume of local anesthetic is mainly based on an ability to observe the spread of the local anesthetic directly **(Latzke et al., 2010).**

Basics of ultrasound physics

Ultrasound is a form of mechanical sound energy that travels through a conducting medium (e.g., body tissue) as a longitudinal wave producing alternating compression (high pressure) and rarefaction (low pressure). Sound propagation can be represented in a sinusoidal waveform with a characteristic pressure (P),wavelength (λ), frequency (f), time (T) and velocity (speed (c) + direction) (Figure14) **(Edler and Lindstrom, 2004).**

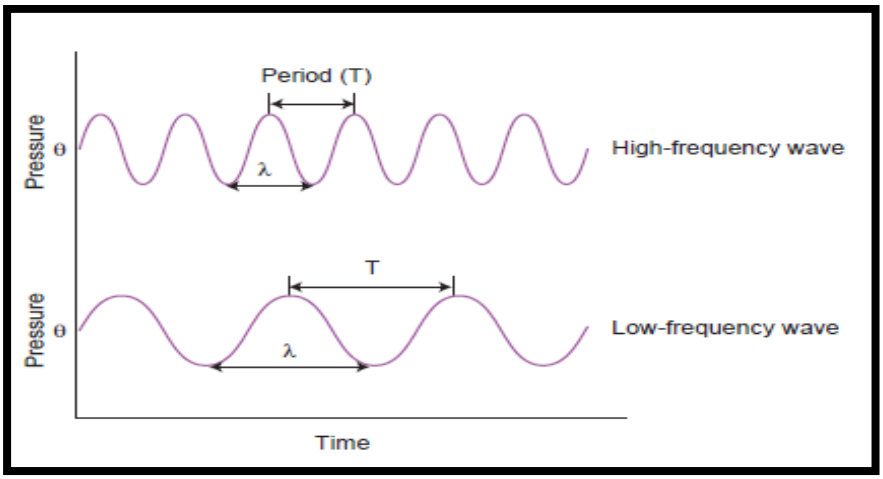

Fig. (14): ultrasound waves**,** High-frequency probes produce shorter wavelength waves, and low-frequency probes produce longer wavelength waves **(Edler and Lindstrom, 2004).**

Tissue appearance under ultrasound:

- **Hyperechoic areas :-** have a great amount of energy from returning echoes and are seen as white.
- **Hypoechoic areas :-** have less energy from returning echoes and are seen as gray.
- **Anechoic areas** without returning echoes are seen as black.

Ultrasound waves and tissue interaction:

The speed of ultrasound waves through biological tissue is based on the density of tissues, and not the frequency of the ultrasound waves. The greater the tissue density, the faster the ultrasound waves will travel. The image processor in the ultrasound machine assumes that the ultrasound waves are travelling through soft tissue at a velocity of 1,540 m/sec. Three things can happen to ultrasound waves as they travel through tissue reflection, attenuation, and refraction **(Weyman, 1994).**

1-Reflection:

The generation of ultrasound images is dependent on the energy of the echoes that return to the probe. The amount of reflection of ultrasound waves is dependent on the difference in acoustic impedance at the interface between different tissues. Acoustic impedance is the resistance of a material to the passage of ultrasound waves (Figure15).The greater the difference in acoustic impedance at tissue interfaces, the greater the percentage of ultrasound waves that is reflected back to the probe to be processed into an image **(Middleton et al., 2004).**

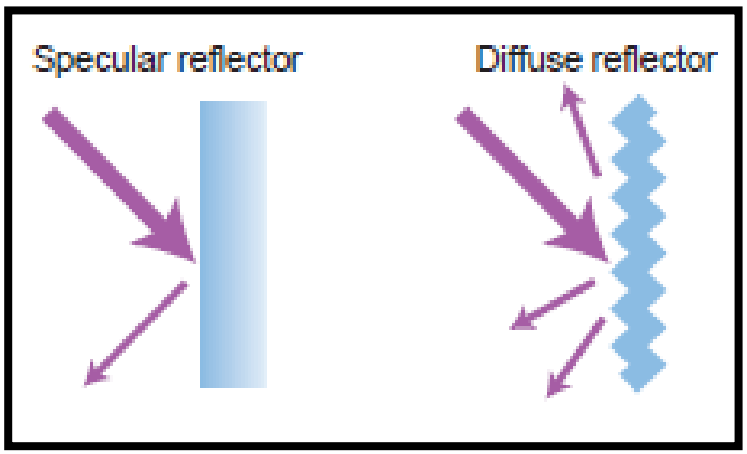

Fig.(15): Specular reflection vs. scattering reflection **(Middleton et al., 2004).**

2-Attenuation:

Attenuation of ultrasound waves is dependent on three factors:

- Attenuation coefficient of the tissue.
- Distance travelled.
- Frequency of the ultrasound waves.

Attenuation is directly related to frequency; the higher the frequency of the ultrasound wave, the greater the attenuation. Therefore, high frequency probes have less tissue penetration due to greater attenuation, which makes imaging of deeper structures difficult with high-frequency probes **(Jespersen, 1998).**

3-Refraction:

When the acoustic impedance between tissue interfaces is small, the ultrasound wave's direction is changed slightly at the tissue interface, rather than being reflected directly back to the probe at the interface this is analogous to the bent appearance of a fork in water, which is caused by refraction of light waves at the air/water inter face. Refracted waves may not return to the probe in order to be processed into an image. Therefore, refraction may contribute to image degradation (Figure:16) **(Otto, 2000)**.

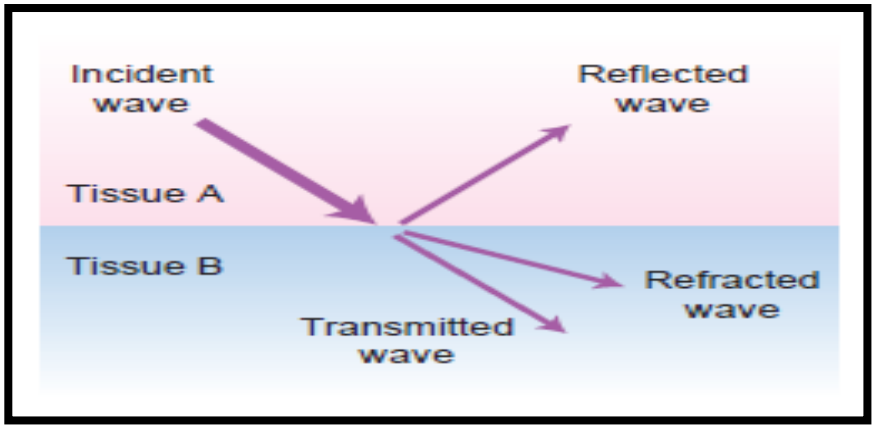

Fig. (16): Refraction vs. reflection **(Otto, 2000)**

Resolution:

It is the ability to distinguish two close objects as separate, is very important in ultrasound-guided regional anesthesia. There are two types of resolution:

- Axial resolution.
- Lateral resolution.

1-Axial resolution:

Axial resolution is the ability to distinguish two objects that lie in a plane parallel to the direction of the ultrasound beam. Axial resolution is equal to half of the pulse length. Higher frequency probes have shorter pulse lengths, which allows for better axial resolution.

The ultrasound probe emits ultrasound waves impulses, not continuously. These pulses of ultrasound waves are emitted intermittently as the probe has to wait and listen for the returning echoes**(Chan, 2009).**

2-Lateral resolution:

Lateral resolution is the ability to distinguish two objects that lie in a plane perpendicular to the direction of the ultrasound beam. Lateral resolution is related to the ultrasound beam width, the more narrow (focused) the ultrasound beam width, the greater the lateral resolution. High frequency probes have narrower beam widths, which allows for better lateral resolution. Poor lateral resolution means that two objects lying side by side may be seen as one object. The position of the narrowest part of the beam can be adjusted by changing the focal zone**(Chan, 2009)**.

Ultrasound machine controls:

1-Depth:

The depth of tissue imaged can be adjusted on the machine and relates to the type of probe being used. Low-frequency probes will be able to image deeper tissue depths than high-frequency probes. With a linear array probe, as the depth is increased, the image on the screen will appear narrower and structures will appear smaller, but the width of the field of view is relatively constant. Notice that the field of view is constant from 3 cm to 6 cm but at 2 cm it has decreased **(Kossoff, 2000)**.

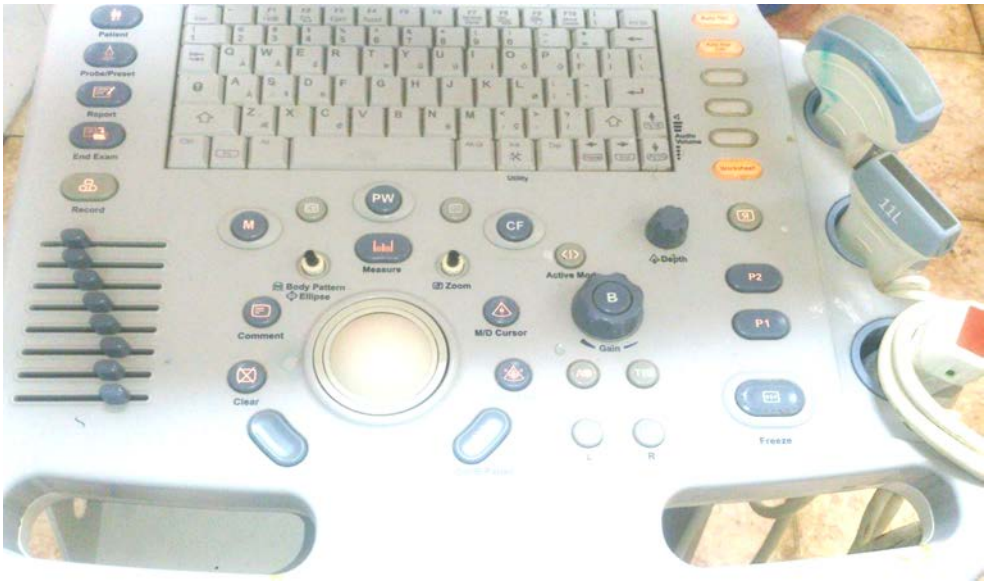

Fig. (17):-General Electric (GE) ultrasound portable device control pannel

2-Frequency:

Variable-frequency probes allow changes in frequency within a narrow range. An 8 to 13 MHz probe allows selection of frequency between 8 and 13 MHz. The lower frequencies are used for deeper structures and the higher frequencies are used for more superficial

structures. Select a frequency that balances penetration and resolution **(Lawrence, 2007).**

3-Gain:

Ultrasound probes transmit ultrasound waves 1% of the time and spend the remaining 99% of the time listening for the returning echoes. Increasing the gain increases signal amplification of the returning ultrasound waves, in this way the gain function can be used to compensate for loss of energy due to tissue attenuation. Returning ultrasound waves are referred to as "signal" while background artifact is referred to as "noise". Increasing the gain increases the signal-to-noise ratio. However, if the gain is increased too much, the screen will have a "whiteout" appearance and all useful information is lost **(Lawrence, 2007).**

4-Color-flow Doppler:

Color-flow Doppler allows for detection of flow within vascular structures. Moving objects, such as red blood cells (RBCs), affect returning ultrasound waves differently than stationary objects. Color-flow Doppler can differentiate between RBCs moving away from the probe and RBCs moving towards the probe. Red blood cells moving towards the probe will return ultrasound waves at a higher frequency and are displayed as red; RBCs moving away from the probe will return ultrasound waves at a lower frequency and are displayed as blue **(Lawrence, 2007).**

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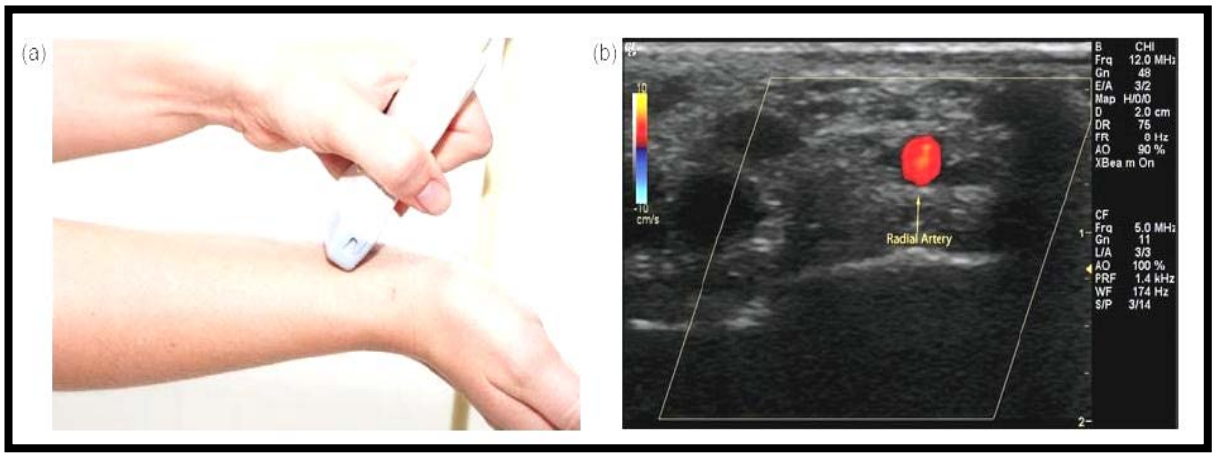


Fig (18): Radial artery flow is seen as red when the probe is tilted towards the direction of flow **(Otto, 2000)**.

5-Pulse-wave Doppler:

Pulse-wave Doppler provides flow data from a small area along the ultrasound beam. The area to be sampled can be selected by the operator. Once pulse-wave Doppler is selected, the image is frozen and the operator selects the area to be sampled. The pulse-wave information is displayed graphically at the bottom of the screen as well as heard(figure 19) **(Otto, 2000)**

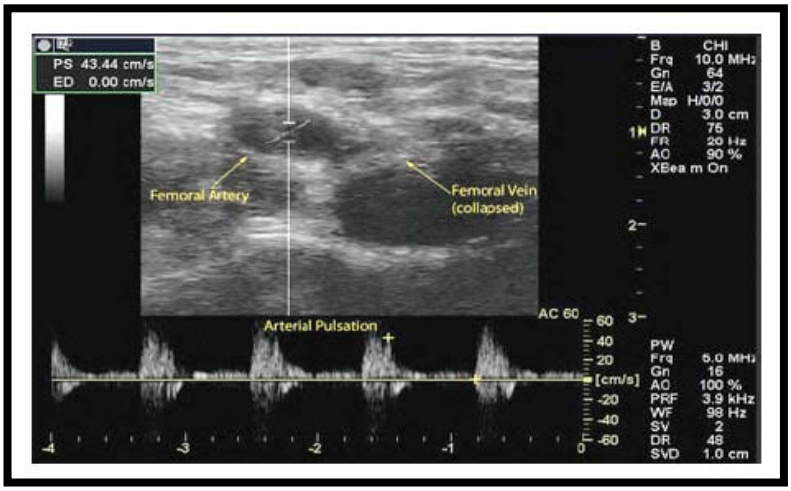


Fig.(19): Pulse-wave Doppler showing arterial flow in the femoral artery **(Otto, 2000)**

Needle insertion:

1-In plane (IP)

The needle is inserted in the same plane as the ultrasound beam. The goal is for the path of the needle to be entirely within the beam of the ultrasound. The more parallel the needle is to the probe (shallower angle of insertion) the easier the needle will be to visualize. When inserting the needle, the goal is to be as close to parallel to the probe as possible. Since with many blocks it will be impossible for the needle to be parallel to the probe, the goal should be to have as shallow an angle of insertion as possible. In order to achieve a shallow angle between the needle and the probe, some blocks will require that the needle be inserted a greater distance from the probe as opposed to right next to the probe**(Chan, 2009).**

2-Out of plane (OOP):

The needle is perpendicular to the beam of the ultrasound. The needle is seen as a small hyperechoic dot on the screen. In an OOP approach, the needle needs to travel a shorter distance to the target than in-plane approach. For those making the transition from nerve stimulation to ultrasound, the location of needle insertion in the OOP approach is similar to the traditional nerve stimulator insertion points. Finding the needle tip in an OOP approach can be challenging for the beginner. The steeper the angle of insertion, the easier to see the needle in an OOP approach**(Chan, 2009)**.

Local Anesthetics

Clinical applications of local anesthetics range from local infiltration or application to allow painful procedures, to peripheral or neuraxial nerve blocks to relieve acute or chronic pain, to intravenous injection to treat cardiac arrhythmias or pain. The development of modern organic chemistry enabled the synthesis of the first analogue of cocaine, procaine (known today by its trade name Novocaine) in 1905 was not without problems, however, including a very long onset time, short duration, and low potency. Cocaine and procaine are both ester local anesthetics. A breakthrough came in the 1940s when the Swedish pharmaceutical company Astra introduced lidocaine (Xylocaine) **(Ruetsch et al.,2001).**

Table (3) Different Nerve fibers: Characteristics and Sensitivity to Local Anesthetics:

FIBER	DIAMETER, μm	CONDUCTION SPEED, M/SEC	SENSITIVITY TO BLOCK	MYELINATION	ANATOMIC LOCATION	FUNCTION
A-α	15-20	80-120	++	+++	Afferent and efferent from muscles and joints	Motor, proprioception
A-β	8-15	80-120	++	+++	Afferent and efferent from muscles and joints	Touch, pressure, proprioception
A-γ, A-δ	3-8	4-30	+++	++	Efferent to muscle spindles, sensory roots, and afferent peripheral nerves	Pain, temperature, touch/motor
B	4	10-15	++++	+	Preganglionic sympathetic	Autonomic—preganglionic
C	1-2	1-2	++++	-	Postganglionic sympathetic, sensory roots, and afferent peripheral nerves	Pain, temperature, touch

(Goodman et al., 1996).

Pharmacodynamics:

Anatomy of Nerves:

The surface of the nerve axon is formed by the lipid bilayer membrane that is embedded with various proteins including ion channels. Myelinated nerve axons are surrounded by Schwann cells. Schwann cells produce myelin that wraps around the axons to form the *myelin sheath*. When seen lengthwise, the myelin sheath is punctuated by gaps called *nodes of Ranvier*. Other axons such as postganglionic autonomic efferent and some of the nociceptive afferent fibers lack a myelin sheath (Figure 20). Nerve axons are further organized within three layers of connective tissue: the endoneurium, perineurium, and epineurium.

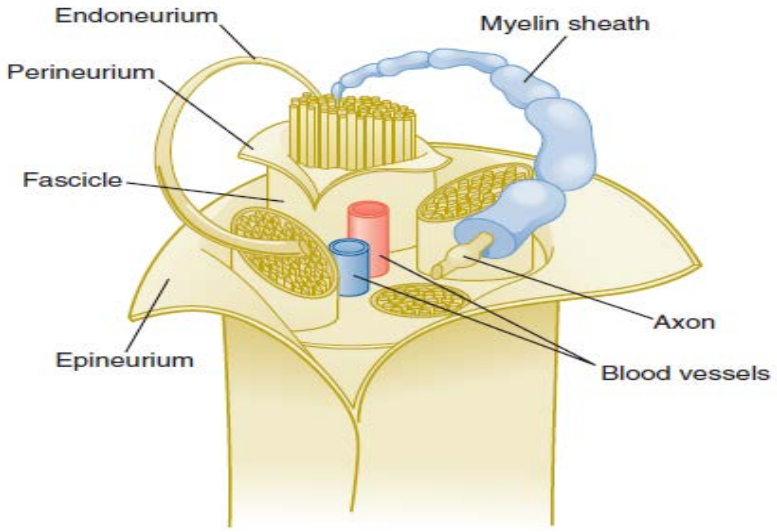


Fig. (20):- Schematic diagram of nerve structure **(Marieb and Hoehn, 2007)**

Voltage-Gated Na+ Channels and Their Interaction with Local Anesthetics:-

Ion channels are multi-subunit transmembrane proteins that fold in a complex manner to form ion selective pores gated by voltage or ligands. Ion channels can switch between different conformations in a voltage

dependent manner that determines pore opening (activation), closing (inactivation), and reactivation (to the resting state) (Figure 21).

Voltage-gated Na+ channels consist of a single **α**-subunit and varying auxiliary **β**-subunits. The **α** subunit forms the ion-conducting pore of the channel and consists of four homologous domains, each with six **α**-helical transmembrane segments (Figure 22).

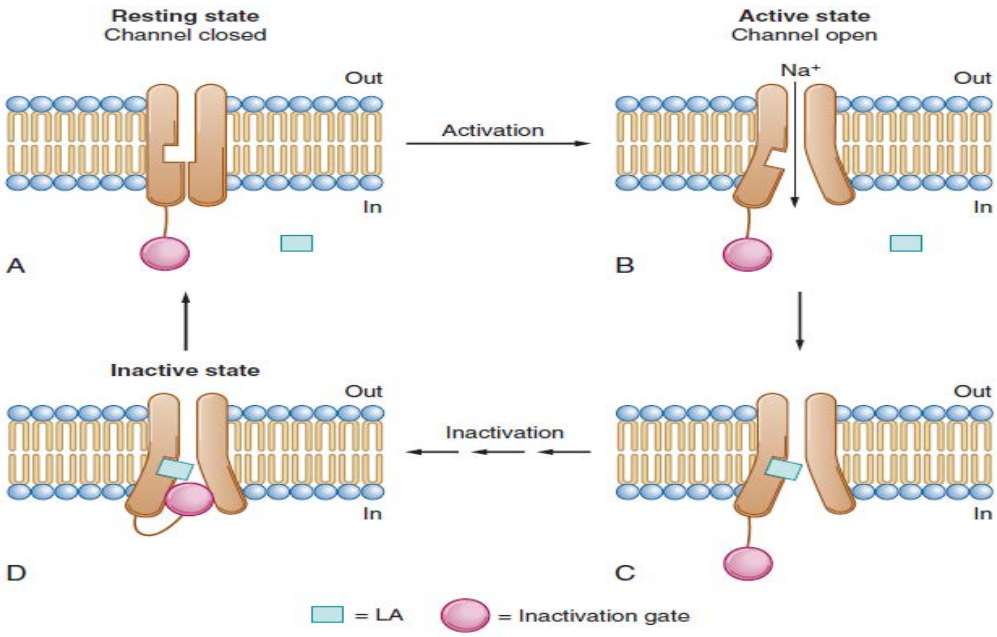


Fig. (21): Different states of voltage-gated Na+ channel. **(Ulbricht, 2005).**

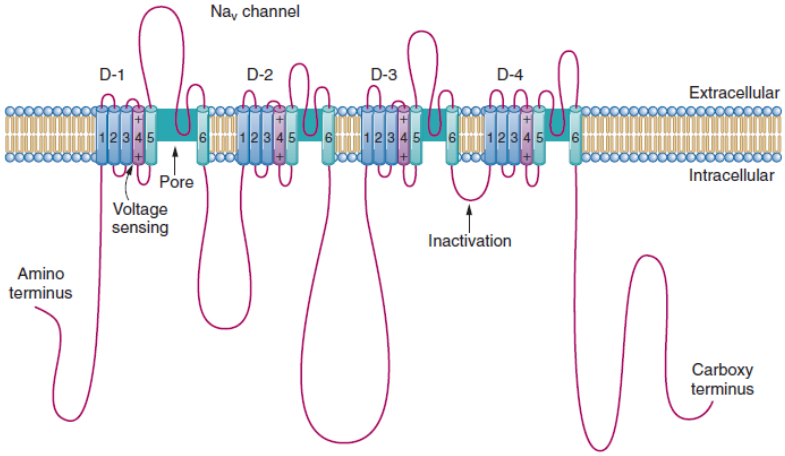


Fig. (22):- Schematic structure of voltage-gated Na+ channel α-subunit. **(Ulbricht, 2005).**

The loops that connect the S5 and S6 segments of these α-helices of each of the four domains are positioned extracellularly and extend inward, which form the narrowest point of the channel pore and are thought to provide its ion-selectivity .In the resting state, the ion pore of the Na+ channel is closed. Depolarizing voltage changes lead to movement of the voltage sensor (S1-S4) due to outward movement of positive charges in the S4 segment, which in turn leads to the rearrangement of S6 segments that result in opening of the channel pore. The activated channel is inactivated within milliseconds by another conformational change, resulting in the movement of the S6 segment and the S5-S6 linker acting as an inactivation gate. The inactivated state differs from the resting state in its molecular conformation as well as its interaction with local anesthetics, which selectively bind and stabilize the inactivated state. Local anesthetics dose-dependently decrease peak Na+ current through voltage-gated Na+ channels **(Ulbricht, 2005).**

Mechanism of Nerve Block:

Only a very small fraction (1%-2%) of local anesthetic reaches the nerve membrane even when placed in close proximity to the nerve . The quality of nerve blockade is determined not only by the potency of the individual local anesthetic, but also by the concentration and volume of the local anesthetic. The potency of a local anesthetic can be expressed as the minimum effective concentration (MEC) at which complete nerve block is established. The volume of local anesthetic is also important as a sufficient length of axon must be blocked in order to prevent regeneration of the impulse in the adjacent node of Ranvier. This is understood by the phenomenon of decremental conduction whereby depolarization of the membrane decays with the distance away from the front of the action potential, and impulse propagation stops when the depolarization falls

below the conduction threshold .If less than the critical length of the axon is blocked, the action potential can be regenerated in the proximal membrane segment or node when the decaying depolarization is still above threshold for Na+ channel activation **(Popitz&Bergez et al.,1995).**

Differential Block:-

Different nerve types show varying susceptibility to nerve block. Displays the characteristics of different nerve types. Clinically, sensory functions are blocked before motor function. This differential nerve block was initially attributed to differences in axon size. Nociceptive-selective nerve block (differential block) has been attempted with concentrations of local anesthetics that are just high enough for only certain nerve fibers (smaller diameter, thinly myelinatedA**δ** or unmyelinated C-fibers), but not for others (larger diameter, myelinated nerves such as A**β**). Nevertheless, nerve block does not always follow this size principle in that A**γ** is blocked at lower concentration than C fibers and myelinated fibers before unmyelinated fibers **(Gokin et al.,2001).**

Pharmacokinetics:

The plasma concentrations of local anesthetics are determined by intravascular absorption, distribution, biotransformation, and excretion. All of these are affected by patientfactors such as age, body size, and organ function. Therefore clinical data must be synthesized with the pharmacology ofthe local anesthetics in order to predict overall pharmacokinetics in each individual.

Absorption

The rate and extent of systemic absorption of local anesthetic depend on multiple factors: site of injection, dose, physiochemical

properties of the drugs, and presence of vasoconstrictive or other adjuvants. Injection in a more vascular tissue results in higher plasma concentration of local anesthetic in a shorter time. Thus a given dose of local anesthetic that can be administered safely for one type of block can result in higher plasma levels and potential systemic toxicity in another type of block. Clinically, the order of decreasing rate of systemic absorption is intravenous, intercostal, caudal, epidural, brachial plexus, femoral, sciatic, and subcutaneous injections. The use of vasoconstrictors such as epinephrine reduces the rate of systemic absorption as mentioned earlier. The addition of epinephrine to bupivacaine and etidocaine significantly decreases the rate of absorption in brachial plexus block but the effect is minimal when used epidurally **(Ulbricht,2005).**

Distribution

Local anesthetics are distributed throughout the body but their concentrations vary between different tissue types with preference to more vascular tissues. The rate of distribution can typically be described by a two-compartment model with rapid and slow phases. The rapid phase involves uptake in highly perfused tissues reaching rapid equilibration. For example, lung is a major site of uptake for local anesthetic. The slow phase depends on the slow equilibration of less perfused tissues and on specific properties of individual local anesthetics **(Tucker G and Mather L, 2005)**.

Metabolism

The major difference between ester and amide type local anesthetics is their metabolism. Ester type local anesthetics undergo hydrolysis by plasma esterases. An exception to this is cocaine which is metabolized in the liver by carboxylesterase. One of the metabolites of ester type local

anesthetics, PABA, can cause allergic reactions in susceptible individuals. Amide type local anesthetics undergo biotransformation mainly in the liver. The rate of metabolism varies between different agents such that degradation of lidocaine is faster than mepivacaine, whose metabolism is still faster than bupivacaine. The metabolites of amide type local anesthetics are excreted by the kidneys. Prilocaine can be metabolized in the kidney. About 5% of amide type local anesthetics is renally excreted unchanged. Therefore patients with decreased hepatic or renal functions eliminate amide type local anesthetics more slowly and are at increased risk for systemic toxicity. An exception is articaine, which is inactivated by plasma carboxylesterase **(Tucker G and Mather L, 2005)**.

Local anesthesia Toxicity:-

The toxicity of local anesthetics is the limiting factor in their clinical applications. Local anesthetics are relatively safe if administered appropriately. However, significant systemic or localized toxicity can result from unintended intravascular, intrathecal, or intraneural injection or if excessive doses are administered resulting in major systemic absorption **(Rosenberg et al.,2004)**.

Systemic Toxicity

Systemic toxicity manifests primarily in the cardiovascular and central nervous systems.

Cardiovascular System

Local anesthetics affect the cardiovascular system both directly by affecting cardiac myocytes and peripheral vascular smooth muscle cells, and indirectly by actions on the autonomic nervous system. The more

potent, lipophilic local anesthetics such as bupivacaine, tetracaine, and etidocaine are more cardiotoxic than the less lipophilic agents such as procaine, prilocaine, and lidocaine **(Heavner,2002)**.

The action of local anesthetics on peripheral vascular smooth muscle is biphasic with vasoconstriction at low concentrations and vasodilation at higher concentrations. The exception is cocaine, which produces vasoconstriction at any dose **(Johns et al.,1985).**

Indirect cardiovascular effects of local anesthetics are related to the use of neuraxial techniques and include hypotension, bradycardia, and cardiopulmonary collapse if not treated promptly. Mild to moderate symptoms are usually responsive to intravenous fluids and indirect or direct acting adrenergic agents such as ephedrine and phenylephrine. Severe symptoms and complications are associated with high dermatomal level blocks, use of sedatives, delayed recognition of unintentional subarachnoid or intravenous injection, and delayed treatment; these severe complications might require pharmacologic and even mechanical cardiopulmonary support (**Lee et al.,2008).**

Central Nervous System

Central nervous system toxicity manifests initially as anxiety, dizziness, circumoral numbness, lightheadedness, and tinnitus. Objective symptoms include shivering, muscle twitching, tremors, and eventually generalized tonic-clonic seizure. With a high dose intravascular injection, a brief period of early symptoms and seizure can be followed by respiratory depression and respiratory arrest. Factors that increase susceptibility to CNS toxicity include the use of more potent local anesthetics and the concomitant presence of respiratory or metabolic acidosis (by decreasing the convulsive threshold). Respiratory acidosis

also reduces protein binding of local anesthetics, increasing local anesthetic availability for further toxic effects. Elevated PaCO2 leads to cerebral vasodilation and increased delivery of drug to the CNS. However, acidosis promotes amine protonation leading to less diffusion into nerve cells **(Apfelbaum et al., 1985).**

Treatment of Local Anesthetic Systemic Toxicity:

When unintentional intravenous injection of local anestheticis suspected or systemic toxicity is detected, benzodiazepine should be given prophylactically as an anticonvulsant **(Neal et al., 2010)**.

Thepatient should be monitored closely for any early neurologic signs and symptoms. The airway must be protected to prevent aspiration and hypoventilation, and the seizure should be treated promptly with an intravenous anticonvulsant such as diazepam; sodium thiopental or propofol are acceptable alternatives. Appropriate monitoring should be applied to assess cardiovascular and pulmonary function. Hypoventilation and respiratory acidosis should be supported with supplemental oxygen or artificial airway and mechanical ventilation. Hypotension and bradycardia should be treated with intravenous fluids and chronotropes, inotropes, and vasoactive agents. Epinephrine is still considered the mainstayof immediate treatment and the use of vasopressin has also been suggested **(Wolfe and Butterworth, 2011).**

Intravenousadministration of lipid emulsion has been used with immediateand successful resuscitation of patients with refractory local anesthetic induced cardiac toxicity, and is now a part of standardized treatment algorithms **(Neal et al., 2010).**

Based on animal studies and a growing number of human case reports, hospitals and clinics that perform major conduction blockade should keep available for emergency use a supply of Intralipid 20% **(Rosenblatt et al., 2006)**.

Neurotoxicity and other tissue toxicity

Direct neuronal tissue toxicity (e.g., transient neurologic symptoms [TNS] and caudaequina syndrome) has been described with multiple local anesthetics, but the incidence appears to be significantly higher with lidocaine and mepivacaine than bupivacaine, prilocaine, and procaine**.** TNS is characterized by transient hyperalgesia or dysesthesia in the low back, buttocks, and lower extremities following seemingly uneventful spinal anesthesia but without permanent neurologic damage. Risk of TNS is associated with the use of lidocaine, lithotomy position, and ambulatory procedures. The risk increases with dose, but does not appear to correlate with the concentration of local anesthetic because there is no difference in the incidence of TNS with 0.5% and 5% lidocaine. The etiology of TNS is unclear, but direct neurotoxicity can be demonstrated in vitro and in animal models **(Drasner et al.,1994)**.

Symptoms typically respond to nonsteroidal anti-inflammatory drugs and trigger point injections. That the mechanism of neural toxicity is poorly understood is underscored by a recent study in patients demonstrating that intraneural injection of mepivacaine into the sciatic nerve is typically not associated with neural injury **(Zaric and Pace, 2009)**.

Dexmedetomidine:

Dexmedetomidine is a highly selective α-2 agonist similar to clonidine but with a greater affinity for the α-2receptor. Clonidine has a specificity of 220: 1 (α-2: α -1), whereas dexmedetomidine exhibits a specificity of 1620:1. It is the pharmacologically active d-isomer of medetomidine, a full agonist of α-2 adrenergic receptors **(Joseph et al, 2015).**

Cardiovascular Effects:

Dexmedetomidine exhibits a biphasic blood pressure response in a dose-dependent fashion. Intravenous infusion of low doses results in a reduction of mean arterial pressure because of selectivity for central and peripheral α -2 receptors. The resultant decreases in heart rate and systemic vascular resistance indirectly decrease cardiac output and systolic blood pressure **(Ebertet al., 2000)**.

These effects aid in modulating the stress response, promote stability, and may protect against radical fluctuations in cardiovascular parameters intraoperatively. This may be particularly useful in patients at risk for cardiac morbidities who could respond adversely to surgical stressors. Intravenous infusion of high doses or rapid intravenous bolus administration may result in systemic hypertension due to activation of peripheral postjunctional α-1 adrenergic receptors. Dexmedetomidine loses its α -2 receptor selectivity as the dose is increased by intravenous bolus injection or rapid infusion. This loss in selectivity results in an initial increase in blood pressure and concomitant decrease in heart rate, which normalizes within 15 minutes **(Dycket al., 1993).**

Hypertension can also be observed because of the transient activation of peripheral α -2B receptors upon rapid bolus injection of the drug. This brief increase in blood pressure is likely due to an over whelming effect of the competition with vasodilatory effects of the central α-2A receptors .Extreme care should be taken when using dexmedetomidine on patients who are volume depleted or vasoconstricted or who have a severe heart block **(Carollo et al., 2008).**

Respiratory Effects:

A major advantage of dexmedetomidine compared with other anesthetic drugs is its minimal effect on the respiratory system. In patients with poor airway patency, obesity, and/or limited range of motion, dexmedetomidine produces excellent sedation without compromising the airway or depressing respiration **(Joseph et al., 2015).**

Pharmacokinetic Considerations:

Dexmedetomidine conforms to α 2-compartment model of distribution and elimination. It has an elimination half life of 2 hours, but it is a highly lipophilic drug that is rapidly distributed and redistributed, with a distribution half-life of only 6 minutes **(Vennet a.l, 2001)**.

This provides a very rapid onset but a short duration of clinical effect. Its rapid redistribution and elimination make it an acceptable agent for infusion techniques. Dexmedetomidine undergoes direct glucuronidation and CYP2A6-mediated metabolism. Approximately 80–90% is excreted in the urine, and 5–13% is found in the feces.Typically pharmacokinetic-based interactions are unusual **(Kauret al., 2011)**.

However, dosage modifications of simultaneously administered sedatives may need to be made because of drug potentiation. Adding anα-2 agonist to a sedation regimen reduces opioid requirement by 50–75% and benzodiazepine requirement by upwards of 80%.The context-sensitive half-time of dexmedetomidine ranges from 4 minutes after a 10-minute infusion to 250 minutes after an 8-hour infusion (**Kauret et al., 2011)**.

Clinical Considerations:

Dexmedetomidine has 3 main clinical applications: (a) prolonged sedation in hospitalized patients, (b) procedural sedation and general anesthesia, and (c) obtunding emergence delirium. It is used as a sedative agent for critically ill patients requiring prolonged sedation and mechanical ventilatory support in a critical care setting. Dexmedetomidine possesses all of the characteristics of an ideal sedative for intensive care. It lacks respiratory depression, is analgesic and anxiolytic, has a rapid onset is titratable, and produces sedation with hemodynamic stability **(Joseph et al., 2015).**

Secondly, dexmedetomidine is used as an adjunctive sedative agent for procedural sedation. It can be used with agents such as opioids, benzodiazepines, and propofol to enhance sedation and promote and maintain hemodynamic stability. Because it does not produce respiratory depression, it is very useful in patients for whom this would be a concern. Its rapid distribution halflife (6 minutes) and favorable context-sensitive half-time enhance recovery and allow for faster patient discharge **(Kauret al., 2011)**.

However, recovery could be prolonged in cases where infusion of dexmedetomidine continues over several hours. In these cases, the

infusion should be discontinued well in advance of the anticipated discharge time.Dexmedetomidine may be given via bolus injection or continuous infusion. A bolus injection of 0.25–0.5 µg/kg, given slowly in divided doses to avoid a transient increase in blood pressure, produces a noticeable quieting or mellowing effect without respiratory depression. As an alternative, sedation may be induced by a continuous infusion of dexmedetomidine, 1 µg/kg over 10minutes, followed by a maintenance infusion of 0.2-0.7 µg/kg/h (Table4) **(Joseph et al., 2015).**

Finally, dexmedetomidine is very useful in obtunding the emergence delirium sometimes seen after general anesthesia, especially in the pediatric population. It produces profound calming without respiratory depression. This is a major advantage over other drugs that have commonly been used in this situation and deserves further consideration **(Gertler et al., 2001)**.

Table4: Guidelines for use of dexmedetomedine (precedex) in procedural sedation)

Method of Use		*Dose*	
	Circumstances	*Loading Dose*	*Maintenance*
Infusion*†	Adult patients	1 mcg/kg over 10 min	0.6 mcg/kg/h Titrate to effect with doses from 0.2 to 1 mcg/kg/h
	Less invasive procedures	0.5 mcg/kg over 10 min	0.6 mcg/kg/h Titrate to effect with doses from 0.2 to 1 mcg/kg/h
	Patients >65 y	0.5 mcg/kg over 10 min	Reduction in maintenance dosage should be considered
	Patients with impaired hepatic or renal function	A dose reduction should be considered	Reduction in maintenance dosage should be considered
Bolus		0.25–0.5 mcg/kg in slow divided doses	

* Infusion dosing is per manufacturer recommendations.

Precedex Dosing for Procedural Sedation **(Joseph et al., 2015).**

The adverse effects of dexmedetomidine include hypotension, hypertension, nausea, bradycardia, atrial fibrillation, and hypoxia **(Aho et al., 1993; Ebert et al., 2000)**.

Results of some of the recent research identified above have indicated that α2-AR agonists may dose dependently enhance local anesthetic effectiveness and prolong its duration. However, additional possible mechanisms associated with dexmedetomidine that need further investigation to examine its actions in the periphery could be: 1) vasoconstriction around the site of injection (resulting in a delay of the absorption of local anesthetic); 2) prolonged local anesthetic effect possibly by α2-AR agonists interfering with absorption of local anesthetics injected by vasoconstriction since α2-ARs are involved in the control of arterial blood pressure; and 3) nonselective α2-AR agonists create a biphasic arterial blood pressure response (short hypertensive phase and subsequent hypotension). In addition, other investigators have supported another mechanism for the action of α2-AR agonists rather than vasoconstriction, such as a direct effect on peripheral nerve activity **(Kanazi et al., 2006).**

Clonidine has been shown to directly interrupt peripheral nerve action; therefore, the effect of α2-AR agonists may be induced by a direct action toward peripheral blood vessels or peripheral nerves or some component of each **(Gaumann et al., 1992).**

Studies have demonstrated that dexmedetomidine and clonidine enhance local anesthetic action (by peripheral α2-AR). Dexmedetomidine has some advantageous pharmacological characteristics compared with similar sedative medications: 1) hemodynamic stability achieved with dexmedetomidine compared to clonidine is related to the fact that it is

more selective for α2-AR and 2) both baroceptor reflex and heart rate response to a pressor are well preserved with dexmedetomidine. These important findings may suggest that dexmedetomidine has enhanced safety as an adjunct to local anesthetics in patients with cardiovascular disease, compared with other vasoconstrictors (e.g. epinephrine). Dexmedetomidine can result in adverse side effects like hypotension and bradycardia with increased dosage in addition to its effects of sedation and anxiolysis, and further studies are needed to better understand these side effects and the safe optimal dose of dexmedetomidine **(Gaumann et al., 1992).**

Bupivacaine:

Marketed under the brand name **Marcaine** among others, is a medication used to decrease feeling in a specific area. It is used by injecting it into the area, around a nerve that supplies the area, or into the spinal canal's epidural space. It is available mixed with a small amount of epinephrine to make it last longer. It typically begins working within 15 minutes and lasts for 2 to 8 hours **(Whimster and David Skinner, 1997)**.

Possible side effects include sleepiness, muscle twitching, ringing in the ears, changes in vision, low blood pressure, and an irregular heart rate. Concerns exist that injecting it into a joint can cause problems with the cartilage. It is a local anesthetic of the amide group **(Whimster and David Skinner, 1997).**

Medical uses:

Bupivacaine is indicated for local infiltration, peripheral nerve block, sympathetic nerve block, and epidural and caudal blocks. It is sometimes used in combination with epinephrine to prevent systemic absorption and extend the duration of action. The 0.75% (most concentrated) formulation is used in retrobulbar block. It is the most commonly used local anesthetic in epidural anesthesia during labor, as well as in postoperative pain management **(Miller and Ronald, 2006).**

Contraindications:

Bupivacaine is contraindicated in patients with known hypersensitivity reactions to bupivacaine or amino-amide anesthetics. It is also contraindicated in obstetrical paracervical blocks and intravenous regional anesthesia (Bier block) because of potential risk of tourniquet failure and systemic absorption of the drug and subsequent cardiac arrest. The 0.75% formulation is contraindicated in epidural anesthesia during labor because of the association with refractory cardiac arrest **(Ayoub and Coleman, 1992).**

Adverse effects:

Compared to other local anesthetics, bupivacaine is markedly cardiotoxic. However, adverse drug reactions (ADRs) are rare when it is administered correctly. Most ADRs are caused by accelerated absorption from the injection site, unintentional intravascular injection, or slow metabolic degradation. However, allergic reactions can rarely occur **(Ayoub and Coleman, 1992).**

Clinically significant adverse events result from systemic absorption of bupivacaine and primarily involve the central nervous

system (CNS) and cardiovascular system. CNS effects typically occur at lower blood plasma concentrations. Initially, cortical inhibitory pathways are selectively inhibited, causing symptoms of neuronal excitation. At higher plasma concentrations, both inhibitory and excitatory pathways are inhibited, causing CNS depression and potentially coma. Higher plasma concentrations also lead to cardiovascular effects, though cardiovascular collapse may also occur with low concentrations. Adverse CNS effects may indicate impending cardiotoxicity and should be carefully monitored **(Adelaide, 2006).**

CNS: circumoral numbness, facial tingling, vertigo, tinnitus, restlessness, anxiety, dizziness, seizure, coma

Cardiovascular: hypotension, arrhythmia, bradycardia, heart block, cardiac arrest **(Miller and Ronald, 2006)**.

Toxicity can also occur in the setting of subarchinoid injection during high spinal anesthesia. These effects include: parasthesia, paralysis, apnea, hypoventilation, fecal incontinence, and urinary incontinence. Additionally, bupivacaine can cause chondrolysis after continuous infusion into a joint space **(Ayoub and Coleman, 1992).**

Treatment of overdose:

Animal evidence indicates intralipid, a commonly available intravenous lipid emulsion, can be effective in treating severe cardiotoxicity secondary to local anesthetic overdose, and human case reports of successful use in this way **(Weinberg et al., 1998; Rosenblatt et al., 2006)**.

Pregnancy and lactation:

Bupivacaine crosses the placenta and is a pregnancy category C drug. However, it is approved for use at term in obstetrical anesthesia. Bupivacaine is excreted in breast milk. Risks of discontinuing breast feeding versus discontinuing bupivacaine should be discussed with the patient **(Ayoub and Coleman, 1992).**

Mechanism of action:

Bupivacaine binds to the intracellular portion of voltage-gated sodium channels and blocks sodium influx into nerve cells, which prevents depolarization. Without depolarization, no initiation or conduction of a pain signal can occur **(Adelaide, 2006)**.

Thoracotomy Complications

Postoperative pulmonary complications following thoracic surgery:

Pulmonary complications are a major cause of morbidity and mortality during the post-operative period after thoracic surgery **(Lawrence et al., 2006).**

The incidence of post-operative pulmonary complications has been reported to vary between 5% and 80%. The incidence varies between hospitals. Lower rates of complications have been reported in hospitals with a high volume of patients. Higher rates have been reported in hospitals with a lower volume **(Fisher et al., 2002; Dimick et al., 2003)**.

The major cause of perioperative morbidity and mortality in the thoracic surgical population is respiratory complications. The major respiratory complications are atelectasis, pneumonia and respiratory failure. These occur in 15–20% of the patients and also account for the majority of the expected 3–4% mortality **(Nakahara et al., 1988).**

All patients undergoing pulmonary resections should have a pre-operative assessment of their respiratory function taking into account three areas-lung mechanical function, pulmonary parenchymal function, as well as cardiopulmonary reserve. These in fact constitute the ‘three-legged-stool’ of respiratory assessment. Individualised strategy is essential. Surgery for pulmonary malignancies needs specific assessment, taking into account the ‘four M's’-mass effects, metabolic effects, metastases and medications. Certain perioperative interventions such as cessation of smoking and lung physiotherapy have been shown to

decrease the incidence of respiratory complications after thoracic surgery in high-risk patients **(Slinger and Darling, 2011).**

Lateral thoracotomy by itself, even without surgical manipulation can produce changes in lung physiology such as reduction of forced vital capacity (FVC) and functional residual capacity (FRC). It has been reported that FVC and FRC can decrease to < 60% of their pre-operative values on the first post-operative day itself. The return back to normal can take up to 2 weeks. This decline, especially of the FRC causes physiologic shunting leading to hypoxemia **(Nunn et al., 1988).**

Many patients require post-operative ventilation. Low serum albumin concentrations, high American Society of Anesthesiologists physical status scores, history of smoking and prolonged surgery are predictors of likelihood of post-operative pneumonia **(Garibadi et al., 1981).**

Post –thoracotomy complications:

Post-thoracotomy complications can be divided into general complications and complications specific to certain procedures **(Higgins, 2013).**

Complications of specific thoracic procedures:

Complications can be categorised as primarily affecting the airway, parenchyma, pleura and chest wall or cardiovascular system.

Airway bleeding and secretions

The upper and lower airways of patients undergoing lung resection surgery are prone to have accumulation of blood and secretions. It is often difficult to remove these by suctioning through the DLT. Pediatric

sized bronchoscopes may be needed to pass through the narrow lumens of the DLT. In extreme scenarios when the suctioning of blood and secretions becomes absolutely imperative, a larger sized DLT may be needed to replace the smaller one **(Raiten and Blank, 2011).**

Mediastinal emphysema

This is a situation when air accumulates in the mediastinal space. This may be a consequence of alveolar rupture, oesophageal rupture or after thoracic surgery. Patients may present with dyspnea and subcutaneous emphysema. Chest X-ray and computed tomography (CT) scan help in diagnosis. Most often, it does not need any emergency treatment, but a chest tube needs to be inserted when there is evidence of pneumothorax. Being a benign condition, it can be treated expectantly. The patients need to be observed for 24h.However, if it is due to an oesophageal rupture, surgical repair or stenting is required **(Raiten and Blank, 2011; Weissberg and Weissberg, 2004).**

Deep venous thrombosis and pulmonary embolism

Post-pneumonectomy syndrome

Post lung resection pulmonary edema

After lung resection surgery, the appearance of pulmonary edema is a serious complication. This carries a mortality rate of more than 50% **(Slinger, 1999)**.

Phrenic nerve injury

Atelectasis

Bronchospasm

Pleural effusions

Chemical pneumonitis

Postoperative respiratory failure

Post thoracotomy pain syndrome:

Post-thoracotomy pain syndrome (PTPS) is defined as pain along the thoracotomy scar recurring or persisting more than 2 months after surgery **(Merskey and Bogduk, 1994)**.

It has been estimated that PTPS affects 30%–50% of patients. The emphasis in previous research has been on reporting the prevalence of persisting pain and risk factors. Intercostal nerve injury has been proposed as a cause of PTPS, and previous studies have focused on investigating the neuropathic pain component to understand the underlying mechanisms better **(Doan et al., 2014; Maguire et al., 2006).**

Recent studies have used the expressions “sensory changes” or “disturbances” rather than “neuropathic pain component” **(Grosen et al., 2013; Johansen et al., 2016)**.

Techniqesof Block

Technique of intercostal nerve block:

Intercostal neural blockade can be achieved intermittently, continuously, or permanently in one or several segments, depending on the technique used. Careful attention to technique decreases the rate of complication. Percutaneous injection of 2-5ml of local anesthetic in at least three adjacent levels will ensure anesthesia/analgesia in the distribution of the middle intercostal nerve because of collateral innervations. Although relief is temporary, this technique is very effective in alleviating somatic pain in the chest wall and abdominal wall. Prolonged blockade requires either multiple reinsertions with the attendant risk of pneumothorax, placement of a catheter for bolus dosing or continuous infusion, injection with a neurolytic agent, or cryoablation **(Debreceni et al, 2003).**

Another important risk to keep in mind is local anesthetic toxicity. Blood levels of local anesthetic after intercostal blockade and interpleural analgesia are significantly greater than after any other frequently performed regional anesthetic techniques. Tucker et al. performed epidural, caudal, intercostal, brachial plexus, and sciatic/femoral nerve blocks with a single injection of mepivacaine 500mg (1% and 2%solutions) with and without epinephrine. When measuring arterial plasma levels, the highest levels were found after intercostal nerve blocks without epinephrine (5-10 microgram/ml). When epinephrine was added to the solution (1:200,000 concentration), the plasma level decreased to 2-5 microgram/ml. Epinephrine should be uniformly added to local anesthetic for performance of intercostal nerve block to minimize the potential for systemic toxicity **(Tucker et al., 1972).**

Posterior approach:

Traditionally, intercostal nerve blocks are performed with a posterior approach at the angle of the rib, 6-8cm lateral to the respective spinous process. This target point allows direct palpation of the rib in most patients. It also allows blockade of the lateral intercostal cutaneous branch, which usually originates distal to the angle of the rib, ensuring good medial as well as lateral analgesia. The immediately adjacent intercostal nerves must also be blocked, because there is collateral innervation from the levels above and below. Neurolytic injections and cryoablative procedures must also be performed in a similar manner **(Nunn and Slavin, 1980).**

Lateral approach:

A variation of this technique is entry at the posterior or midaxillary lines. These approaches may be adequate for blocking the anterior chest or abdominal wall, but will often miss the lateral cutaneous branch, thus providing less than satisfactionary blockade of the back and flank regions. In patients undergoing thoracotomy, the surgeon may perform the blocks under direct visualization just before closure. However, these blocks are often placed at a site more medial than what would be chosen for a percutaneous approach. Thus, there seems to be a higher incidence of complications because of the spinal nerve roots **(Nunn and Slavin, 1980).**

Continuous technique:

Nunn and Salvin described the ability of a single intercostal injection of India ink to spread subpleurally to multiple intercostal spaces. The minimally adherent parietal pleura and the thin intercostalisintimus

muscle did not hinder the multidirectional spread of the injectate. Based on morphometric measurements of intercostal space**. Nunn and Slavin** placed the needle tip 3mm past the inferior margin of the rib, leaving approximately 5mm to the pleura. In a study by **O'Kelly and Garry**, a continuous catheter was placed through a 19-gauge epidural needle with the tip directed medially. After first injecting 10 ml of solution through the needle, catheter was advanced 2cm and then secured to the skin. Appropriate spread of local anesthetic was confirmed by radiographic imaging **(Nunn and Slavin, 1980; O'Kelly and Garry, 1981).**

Satisfactory analgesia has been documented using continuous infusion. Seventy five patients (92%) have good analgesia without requiring supplemental medications during the first postoperative day using an infusion of 0.5% bupivacaine at 7ml/hour. Sixty-six patients (81.5%) remained satisfied with their analgesia over the following 4 days. Patients who experienced inadequate analgesia early in their course were thought to have leakage of anesthetic into the interpleural space. Subsequent decrements in analgesic efficacy were attributed to tachyphylaxis. The same authors modified the protocol to increase the infusion rate to a maximum of 10ml/hour. This resulted in a significant improvement in pulmonary function over the control group, which required higher doses of intravenous rescue pain medications than the continuous intercostal infusion group (**Sabanthan et al., 1988; Sabanthan et al., 1990).**

Ultrasound guidance may decrease the chance of intravascular injection, pneumothorax and allows injection closer to the midline than anatomic landmarks. This increases the chance that injection is made before the division of the lateral branch which is necessary to achieveanesthesia of the entire intercostal dermatome. The individual ribs

to be blocked should be marked out as with the landmark technique. The ultrasound probe is then placed in a sagittal plane about 4 cm lateral to the spinous process. The ribs are visualized as a shadow while the pleura and lung are visualized anterior to the intercostal space. The needle can then be inserted in or out of a plane to the transducer and advanced until the tip is just below the inferior border of the rib. After negative aspiration, 3 to 5 mL of local anesthetic is injected, and the pleura should be visualized being pushed away **(Bhatia et al., 2013).**

As in the use of line placement, ultrasound technology is being used by physicians other than radiologists for visualization during invasive therapeutic or diagnostic procedures such as intercostal nerve blocks (INBs). The thoracic wall poses certain challenges because of its unforgiving anatomy and the morbidity associated with complications **(Narouze and Peng, 2010).**

While a **2006** study noted concerns about the accuracy of needle placement in identifying the correct thoracic level. Furthermore, when identifying bony landmarks are absent because of body habitus or when anatomy has been altered because of traumaor surgery, or in high-risk situations when patients are receiving anticoagulant therapy, guidance is key. Hence, current practices for procedures involving the thoracic wall are typically performed under fluoroscopic guidance for needle placement **(Chiodo et al., 2006).**

Needle insertion approach:

Ultrasound guided posterior intercostal nerve block is considered a BASIC skill level block (Level 1) .The only major risk is pneumothorax should the needle puncture the pleura **(Petal and Joshi, 2013).**

For posterior intercostal nerve block, the ideal needle insertion site is the ICS **lateral** to the costal angle and posterior to the posterior axillary line (because the neurovascular bundle has not yet divided) **(Narouze et al., 2012).**

An out-of-plane approach, with direct access to the intercostal space, as well as an in- plane technique is possible. With the in-plane approach, a transducer with a small foot print is required (Figure 23). The in-plane approach has the advantage of visualizing the block needle more clearly but the passage may be partially obstructed by the rib one space below. This is true especially in case of narrow ICSs **(Narouze et al., 2012).**

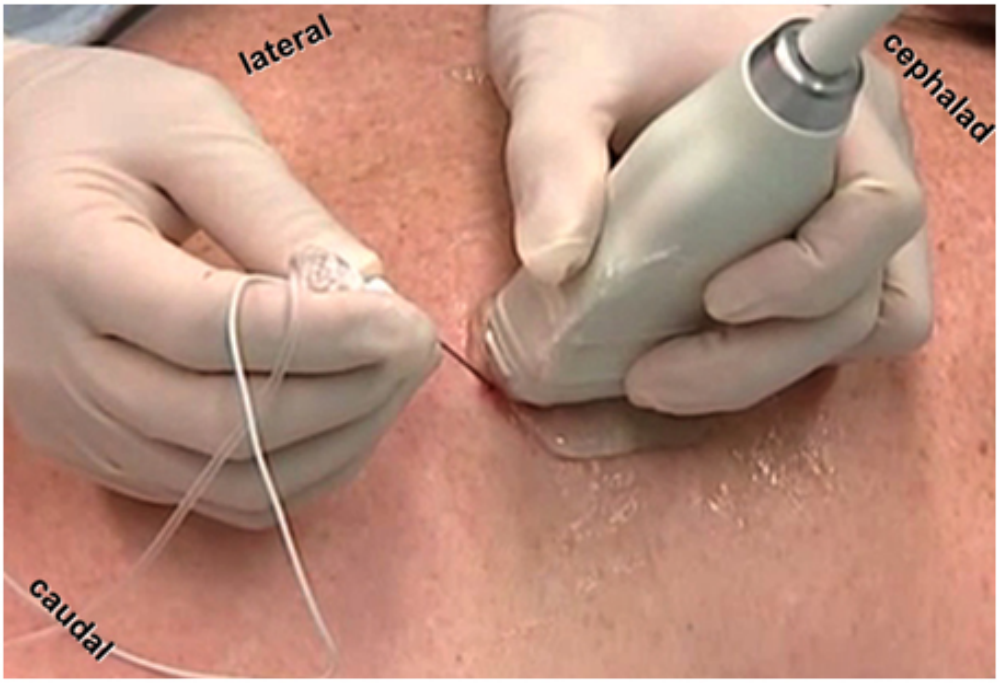


Fig. (23): In plane needle advancement from caudad to cephalad (Narouze et al., 2012).

With either needle approach, it is important to hydrodissect repeatedly during needle advancement in the tissue plane before reaching the internal intercostal muscle. This will facilitate visualization of the needle tip and identify the correct tissue layer **(Vandepitte et al., 2013).**

With the patient lying prone, a 22 G, 3.5 or 5 cm needle is advanced to penetrate the external and internal intercostal muscles (Figure 24). The optimal target needle endpoint is a location just within the internal intercostal muscle to assure that the needle tip remains superficial to the parietal pleura. Again, the innermost intercostal muscle is not always visualized thus is not a useful landmark to guide injection. The clearly visible internal intercostal muscle serves an indirect sonographic target for needle insertion **(Stone et al., 2011).**

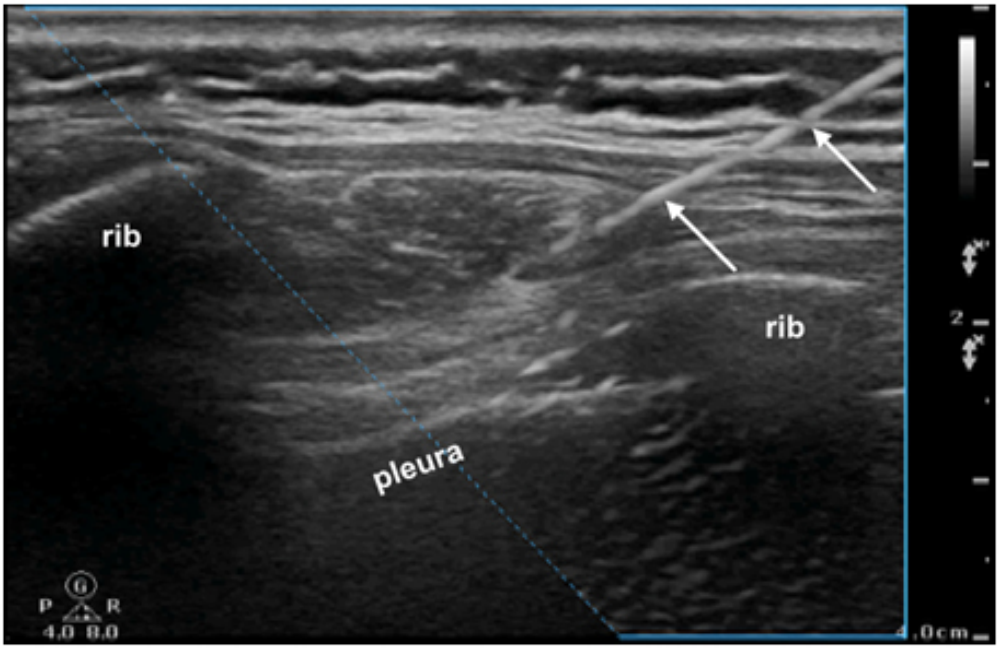


Fig. (24): Sonogram showing needle using an in plane insertion approach (Vandepitte et al., 2013).
arrows =blockneedle

The needle should **not** traverse the parietal pleura to avoid pneumothorax. Perform a post block ultrasound scan to rule out pneumothorax. The absence of comet tail artifacts and sliding pleura indicates pneumothorax **(Stone et al., 2011).**

Complications of intercostal nerve block:

The most common complications of intercostal nerve block are associated with the aberrant needle placement (pneumothorax, hemothorax, hemoptysis, hematoma, intravascular injection, neuritis, subarchinoid block, failed block) or problems associated with the injectate (allergic reaction, toxic reaction, epinephrine reaction, tissue necrosis, respiratory insufficiency). The actual incidence of pnuemothorax secondary to intercostal nerve block is quite small. **Alarge**, retrospective study reporting 50,097 intercostal nerve blocks in 4333 patients undergoing surgery or therapeutic nerve blocks revealed only for clinically significant pneumothoraces (0.092%) and no other significant complications **(Moore, 1975).**

Motor blockade and the loss of accessory respiratory muscle function were the hypothesized etiologic mechanisms. In a study looking at the efficacy of continuous epidural versus intercostal analgesia, one intercostal catheter led to rib osteomyelitis which had to be treated surgically **(Debreceni et al., 2003).**

Intraoperative intercostal nerve block performed by the surgical team has resulted in total spinal anesthesia. Presumably, this serious complication occurred because of the proximity of the injections to spinal nerve roots. Paravertebral neural block has also occurred with attempted intercostal nerve block during surgery**(Berrisford and Sabanatban, 1990).**

Intrapulmonary injection is a risk, especially when there has been an alteration in the pulmonary anatomy secondary to previous surgery. Acute bronchospasm from intrapulmonary injection of 8% phenol has

been reported. The characteristic odor of phenol was detected in the patient's exhaled air **(Atkinson and Shupak, 1989).**

In addition to the issue of epidural blockade with continuous intercostal neural blockade, there is concern regarding misplacement of the catheter. The actual technique of catheter placement is somewhat imprecise, lacking a definitive end point. **Mowbrayet al**, performed intercostal catheterization in 22 patients scheduled for thoracotomy or median sternotomy. At the time of surgery, it was found that only 12 catheters (54.5%) were actually placed correctly in the intercostal space. Catheter dislodgment and interpleural or intravenous catheter migration can occur. Relative contraindications to intercostal blockade include patient refusal, history of allergic reaction to injectates, coagulopathy, and infection at the proposed site of injection **(Mowbray et al., 1987)**.

Technique of thoracic paravertebral block:

Thoracic paravertebral block (TPVB) is the technique of injecting local anesthetic adjacent to the thoracic vertebra close to where the spinal nerves emerge from the intervertebral foramina. This results in ipsilateral somatic and sympathetic nerve blockade in multiple contiguous thoracic dermatomes above and below the site of injection **(Cheema et al., 1995; Eason and Wyatt, 1979).**

It is effective in treating acute and chronic pain of unilateral origin from the chest and abdomen. Bilateral use of TPVB has also been described**(Barron et al., 1999; Klein et al., 2000).**

Several different techniques exist for TPVB. It can be performed with the patient in the sitting, lateral, or prone position. The sitting position allows easy identification of landmarks, and the patients are

often more comfortable. The classical technique, which is most commonly used, involves eliciting loss of resistance **(Eason and Wyatt, 1979).**

If bone is not encountered at this depth, it is possible that the needle tip is lying between adjacent transverse processes. It is imperative to locate the transverse process before advancing the needle any further to prevent inadvertent deep insertion and possible pleural puncture. This is accomplished by withdrawing the needle to the subcutaneous plane and redirecting it cephalad and caudad to the same depth until bone is encountered. If bone is still not encountered, the needle is advanced a further centimeter and the above process repeated until the transverse process is contacted. The needle is then walked above the transverse process and gradually advanced until a loss of resistance to air or saline, or a subtle "pop" is felt as the needle tip traverses the thin superior costotransverse ligament, usually within 1–1.5 cm from the superior edge of the transverse process **(Eason and Wyatt, 1979).**

After gentle aspiration, local anesthetic is injected in small aliquots or a catheter is inserted so that 1–3 cm of the distal end of the catheter lies within the TPVS. The same technique is used with modification in children, and two simple equations help predict the lateral distance for needle insertion and the skin-to-TPVS depth (both in millimeters):[10.2 + (0.12 × weight in kilograms)] and [21.2 + 0.53 × (weight in kilograms)], respectively **(Lonnquist and Hesser, 1994; Lonnquist and Richardson, 1999)**.

Unlike epidural space location, where a definite give is felt as the needle tip traverses the firm ligamentumflavum, TPVS location using loss of resistance is subjective and indefinite and may not be appreciated as a

definite give**(Richardson and Lonnqvist, 1998; Richardson et al., 1996).**

Difficulty is also commonly encountered during catheter insertion and may require manipulation of the needle or injection of saline to create a saline-filled cavity before passing a catheter. Very easy passage of the catheter may indicate interpleural placement **(Johnson, 1993).**

The needle may be advanced by a fixed predetermined distance (1–2 cm) once the needle is walked off the transverse process without eliciting loss of resistance. This variation has been used very effectively with low risk of complication, including pneumothorax **(Greengrass et al., 1996; Coveney et al., 1998).**

Contrast injected into the TPVS produces either a longitudinal or a cloud-like spread localized to the paravertebral region as depicted on frontal chest radiograph. Radiologic images are not always readily identifiable, and spread can vary in the same patient having repeated injections **(Richardson et al., 1996).**

A modification of the classical approach is the medial approach in which the needle is inserted 1 cm from the midline and advanced perpendicularly to contact the lamina rather than the transverse process followed by lateral redirection to slip off the lamina into the TPVS. Developed initially to avoid intrathecal injection by directing the needle away from the intervertebral foramen, this approach has been associated with complications relating to dural puncture **(Evans et al., 1981).**

Ultrasound guidance for PVB:

Various positions for probe alignment and angles of approach for needle insertion have been suggested. The authors recommend that a linear probe set at 5 MHz is selected and placed about 5 cm from the midline in a craniocaudal direction. An anatomical survey is carried out and the ribs, posterior (internal) intercostal membrane (PIM), and pleura are all identified (Fig. 25). The probe is then moved medially to show the bony transition from rib to TP (Fig. 26). The TP is always more superficial than the rib **(Conacher and Korki, 1987).**

The pleura will become less distinct at this point, so the probe is angulated laterally to improve the image and measure the distances between the skin, TP, and pleura. The TP can then be marked at the midpoint of the probe **(Conacher and Korki,1987) .**

In the ultrasound-assisted approach, the probe is then removed and the block performed as previously described, using the depth information to improve needle placement. The actual needle to bone distance is usually slightly greater due to tissue compression by the probe **(Conacher and Korki,1987).**

In the ultrasound-guided approach, the needle is inserted into the paravertebral space alongside the probe in an 'out-of-plane' technique. As local anesthetic is injected, the space between the pleura and costotransverse ligament will be seen to expand. This expansion can be followed cranially and caudally to assess the need for additional injections. A catheter can then be inserted and the position confirmed **(Cheema et al.1995).**

Testing the block:

If the patient is to be awake or sedated for surgery, anesthesia should be assessed by the response to pinprick or ice, 10-15 min later. Additional injections can then be performed at the appropriate levels if the block is incomplete **(Cheema et al., 1995).**

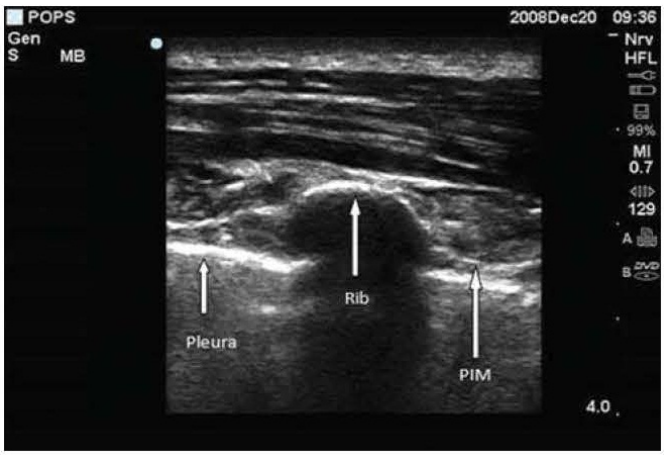


Fig. (25) Ultrasound scan of the chest wall showing the rib, pleura and PIM **(Karmakar, 2001).**

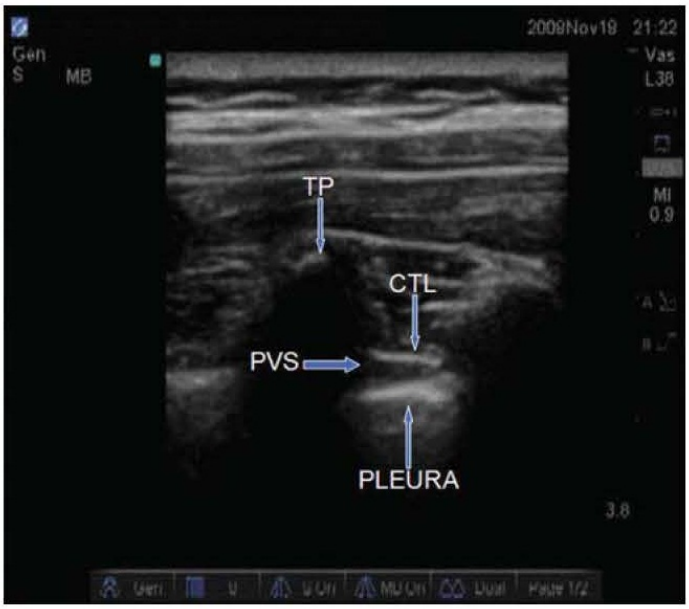


Fig. (26) Ultrasound scan of the posterior chest wall showing the TP, costotransverse ligament (CTL), paravertebral space (PVS), and pleura (Karmakar, 2001).

Failure Rate and Complications

Thoracic paravertebral block is technically easy to learn, has a high success rate regardless of the number of blocks dependent **(Coveney et al., 1998).**

The failure rate varies from 6.8 to 10%, which is comparable with that of other commonly used regional anesthetic techniques and reflects the technical difficulty in accurately identifying the TPVS **(Pusch et al., 1999).**

Based on published data, it is difficult to quote the true complication rate of TPVB, but it appears to be relatively low. **Richardson and Sabanathan** estimated it to be 5%, whereas **Coveney *et* al**. retrospectively reviewed 156 consecutive cases of TPVB using the multiple-injection technique and noted that complications occurred in only four cases (2.6%). **Lönnqvist *et al***. prospectively evaluated complications after paravertebral (thoracic and lumbar) blocks in 367 patients (319 adults, 48 children) and observed the following frequency of complications: vascular puncture, 3.8%; hypotension, 4.6%; pleural puncture, 1.1%; and pneumothorax, 0.5% **(Lonnqvist et al., 1995; Coveney et al., 1998).**

Inadvertent pleural puncture is uncommon and may or may not result in a pneumothorax, which is usually minor and managed conservatively. If it does occur, pleural puncture can be converted to interpleural analgesia. Clues that suggest pleural puncture are a definite pleural "pop" sensation, irritating cough, or sharp pain in the chest or shoulder during the procedure. Air is not aspirated unless the lung is inadvertently punctured or air that may have entered the pleural cavity *via* the needle during removal of the stylet is aspirated. Such

patients need to be closely monitored for the possible development of pneumothorax. Radiologically, interpleural injection (contrast) is seen to move with respiration, does not define any specific anatomical plane, rapidly disperses, and spreads to the diaphragmatic angle or horizontal fissure **(Lonnqvist et al., 1995; Coveney et al., 1998).**

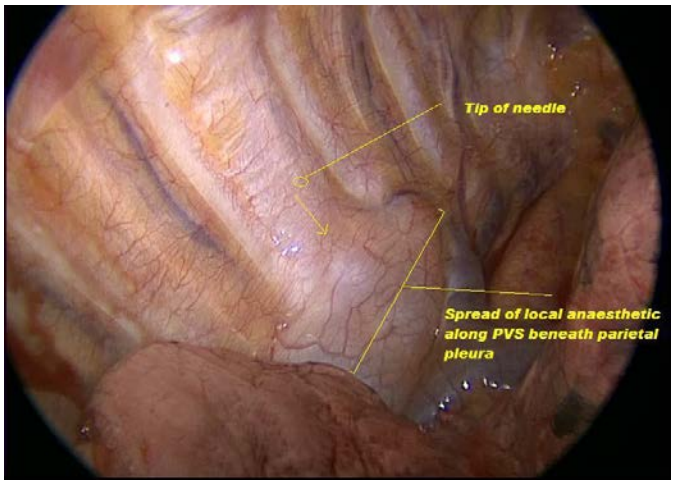


Fig. (27): needle inserted percutaneously from the posterior thoracic wall to tent the pleura **(Mark and John, 2011).**

Pulmonary hemorrhage has been reported after percutaneous TPVB in a patient who had undergone previous thoracic surgery, which highlights the need for caution in patients with altered paravertebral anatomy **(Thomas et al., 1999).**

Hypotension is uncommon after TPVB in normovolemic patients because of unilateral sympathetic blockade, but TPVB may unmask hypovolemia and result in hypotension. Interestingly, hypotension does not appear to be a problem even after bilateral TPVB. Some patients develop hypotension as part of a vaso-vagal episode **(Lonnqvist et al., 1995).**

Transient seizure after inadvertent intravascular and rapid supplementary injection of plain bupivacaine highlights the need to use epinephrine-containing solutions, although this may rarely produce clinical signs of systemic epinephrine absorption**(Coveney et al., 1998).**

Dural puncture–related complications such as intrathecal injection, spinal anesthesia, and postural headache appear to be exclusive to the medial approach to the TPVS and are probably related to the closer proximity of the needle to the dural cuff and intervertebral foramen **(Tenicela and Pollan, 1990).**

Transient ipsilateral or bilateral Horner syndrome can also develop. The former is likely to be caused by spread of local anesthetic to the ipsilateral stellate ganglion or the preganglionic fibers originating from the first few segments of the thoracic spinal cord, whereas the latter may be caused by contralateral paravertebral spread *via* the prevertebral or epidural route **(Pusch et al., 1999; Karmakar et al., 2000).**

Ipsilateral sensory changes in the arm may also develop as a result of spread of local anesthetic to the T1 component of the brachial plexus in the thorax or the C8 component where it originates between C7 and T1, although further spread to the brachial plexus in the neck cannot be excluded **(Coveney et al., 1998).**

Bilateral symmetrical anesthesia and ipsilateral thoracolumbar anesthesia can also occur as described above **(Richardson et al., 1998).**

Segmental thoracic pain that lasted for 3 months after the block may be a result of intercostal nerve trauma during catheter insertion **(Bigler et al., 1989).**

Patients and Methods

- **Ethics Committee:**
  - The study protocol was approved by the institutional ethical committee of Benha university hospitals.
  - Informed patient's written consent was obtained before enrolment in the study.
  - Study was conducted from January 2016 – October 2017.
- **Type of study:**

Prospective, single blind randomized clinical study.

- **Methods of randomization:**

Patients were randomized into two equal groups and each group is subdivided into two equal subgroups. An online randomization program was used to generate random number list. Patient randomization numbers were concealed in opaque envelops which were opened by the study investigator.

- **Methods of blindness:**

Members of the study group involved in obtaining functional data were blinded to randomization for the period of data acquisition and analysis

- **Inclusion Criteria: -**
  - **a-** Age from 20 to 60 years .
  - **b-** ASA physical status: I and II .
  - **c-** BMI between 18.5 and 30 kg m^2
  - **d-** Type of operation: Patients undergoing elective thoracotomy ie: lobectomy operations.

- **Groups allocation:**

Sixty Patients were randomly allocated into two equal groups:-

Group I:-(including 30 patients)

Will receive ultrasound continuous intercostal nerve block this group will be subdivided into:

-**Group Ia(15 patients):** Will receive 15 ml of bupivacaine 0.5% followed by bupivacaine 0.25% at a rate of 0.1 ml/kg/6hrs for 24 hours.

-**Group Ib (15 patients):**Will receive 15 ml of (bupivacaine 0.5%+1microgram/kg dexmedetomidine) followed by (bupivacaine 0.25% + 1 microgram/kg dexmedetomidine) at a rate of 0.1 ml/kg/6hrs for 24 hours.

Group II :-(including 30 patients)

Will receive ultrasound continuous thoracic paravertebral nerve block this group will be subdivided into:

Group IIa(15 patients): Will receive 15 ml of bupivacaine 0.5% followed by bupivacaine 0.25% at a rate of 0.1 ml/kg/6hrs for 24 hours.

Group IIb(15 patients): Will receive 15 ml of (bupivacaine 0.5%+1microgram/kg dexmedetomidine) followed by (bupivacaine 0.25% + 1 microgram/kg dexmedetomidine) at a rate of 0.1 ml/kg/6hrs for 24 hours.

Exclusion criteria:

1- Empyema or neoplastic mass occupying paravertebral or intercostal space.
2- Kyphoscoliosis.
3- History of cerebrovascular disease, seizures or central nervous system disease.

4- Patients with bleeding diathesis.
5- Patients with known allergy to the used drug .
6- Conduction abnormalities.
7- Patients with renal or liver impairement.
8- Patients with psychiatric illness.
9- Patients with local skin infections.

Preoperative visit :-

One day before surgery all patients were interviewed toobtain the following data:

1) Arterial blood gases (PO2,PCO2 and SaO2 levels).
2) Blood cortisol level.
3) Pulmonary function tests (FEV1,FVC,PEFR) values all at rest and at cough (deep breathing).
4) Hemodynamics (arterial blood pressure,heart rate and ECG).
5) Complete blood count (CBC).
6) Coagulation profile (prothrombin time, partial thromboplastin time and international normalized ratio).
7) Liver and kidney functions.

Also to explain visual analogue scale (VAS) from 0 to 10 where 0 (no pain) and 10 (unbearable pain).

It is designed to present to the respondent a rating scale in which the respondents mark the location on the 10-centimeter line corresponding to the amount of pain they experienced. This gives them the greatest freedom to choose their pain's exact intensity. It also allows for each respondent to express a personal response style).

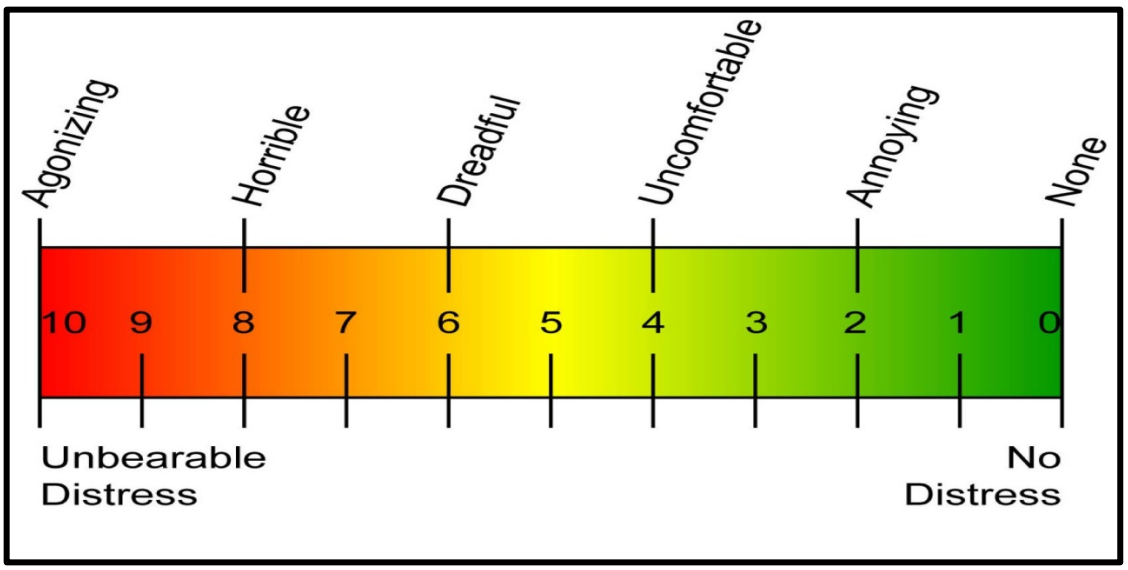


Fig. (28): visual analogue scale

Patients of both groups were transferred to the premedication room. In the premedication roomintravenous access was established and a dose of midazolam 0.05 mg/kg 30 minutes before the operation was adminstered and IV fluid (500 ml of ringer lactate preload) started then the patients were transferred to the operating room where the deficit of fluids was calculated and started in the form of (2/3 ringer lactate and 1/3 dextrose 5%) monitoring of the patients in the form of 5-Lead ECG, arterial blood pressure (non invasive blood monitoring) and pulse oximeter were conducted.

In both groups after pre-oxygenation with 100% oxygen for 3-5 minutes, induction of general anesthesia was done with propofol 2 mg/kg followed by rocuronium 0.6 mg/kg to facilitate endotracheal intubation with cuffed endotracheal tube and isoflurane of 1.2%.

Then arterial cannulation was done together with central venous line in the internal jugular vein by 2-3 single lumen 14-16 gauge catheters or multilumen iv catheters. One iv port for drug infusion and fluids,one for iv boluses and another one for CVP monitoring.

Anesthesia was maintained with isoflurane 1.2%, rocuronium 0.2 mg/kg as a maintenance dose every 30 minutes, fentanyl infusion at a rate of 1microgram/kg/hour and ketorolac 0.1 mg/kg/hour which were discontinued half an hour before extubation.

Ventilation parameters were adjusted as follows:TV=8ml/kg, RR=12/min and peak inspiratory pressure 30-50 cm H2O to maintainend tidal CO2 between 35-40 mmHg.

Calculating the maintenance dose of fluids was done after completion of the patient deficit in the form of (2/3 ringer lactate and 1/3 dextrose 5%) which was divided along the hours of operation.

Intraoperative problems was recorded in the form of hypotension which was treated with intravenous ringer solution 15 ml/kg and ephedrine 10 mg as needed to keep MAP more than 65 mmHg. Hypertension which was treated by increasing depth of anesthesia and vasodilators. Arrythmias which was treated according to the type. Bradycardia (HR<60/min) will be treated with atropine 0.01-0.02 mg/kg and blood loss was assessed.

At the beginning of the operation hemodynamics of the patient will be measured immediately post induction, after skin incision and after rib retraction.

After skin closure the patient was transferred to the lateral position and technique was performed.

Regional block techniques:-

The ultrasound used for the block in all groups, we have used (General Electric; GE , " LOGIQ P5" ultrasound machine) with 5 -12 MHz probes.

A - Technique of continuous intercostal nerve block:-

Patient position:

The patient was positioned in the lateral position .It is helpful to have the patient's spine arched with the arms extended forward to perform the midaxillary technique.

Landmarks:

The following anatomic landmarks are used to estimate the position of the relevant ribs:

1. Twelfth rib (last rib palpable inferiorly)

2. The 7th rib (lowest rib covered by the angle of the scapula)

Once identified by palpation, the inferior border of the corresponding ribs can be marked on the skin. An “x” at the angle of the rib identifies the site of needle insertion, usually about 6-8 cm from the midline. For thoracotomy, an estimate of the levels required for effective analgesia can be made after discussion with the surgeon as to the planned approach and length of incision. Typically, in addition to the estimated dermatomal levels, one additional level above and one below the estimated levels are also blocked.

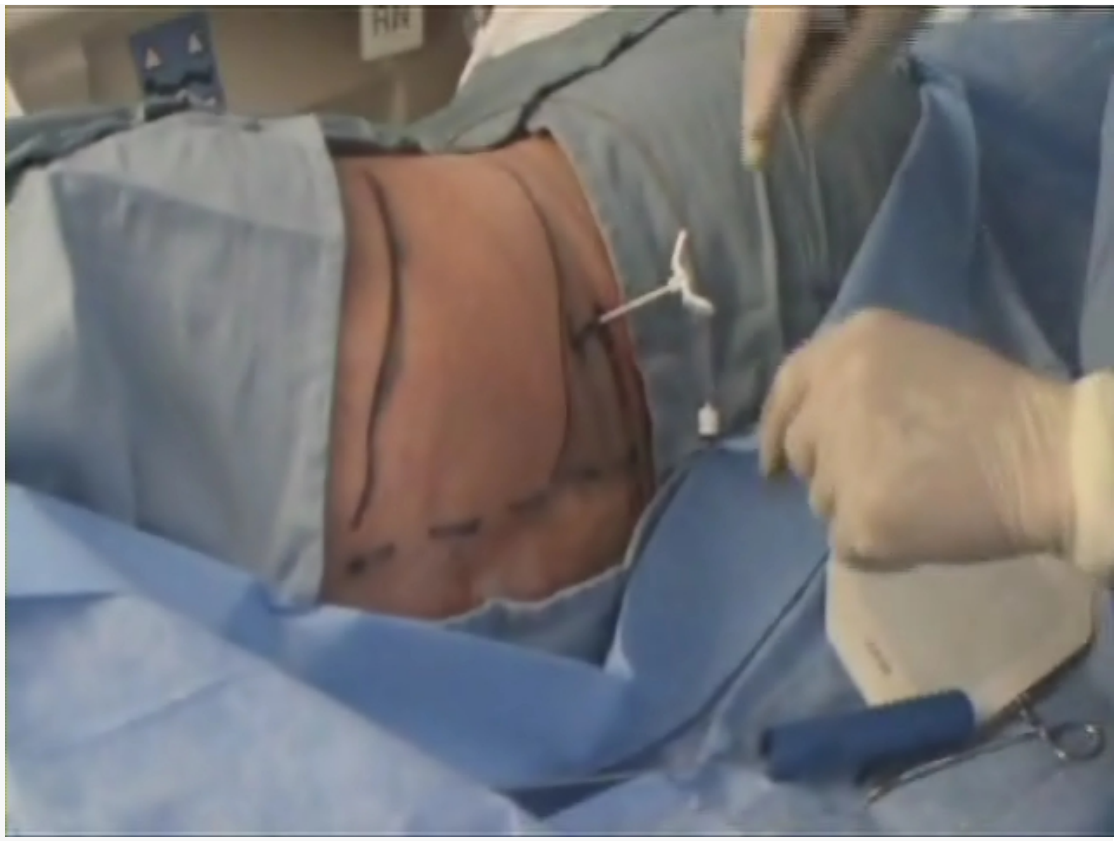


Fig. (29) : Landmarks for intercostal space are identified first by determining the midline and the spinous processes (skin marks). Intercostal space is then determined by palpation at each level to be blocked, and then the insertion point for needle is marked 5-7cm lateral to the midline.

Equipments:

A standard regional anesthesia tray was prepared with the following equipment:

- Sterile towels and 4"x4" gauze packs
- 20-mL syringes with local anesthetic.
- Sterile gloves, marking pen and surface electrode.
- One 1½" 25-gauge needle for skin infiltration
- An 18 gauge 8 cm epidural needle (Perifix. B. BRAUN Melsungen AG)**(Figure 30)**

- GE LOGIQ P5 ultrasound machine **(figure 31)**

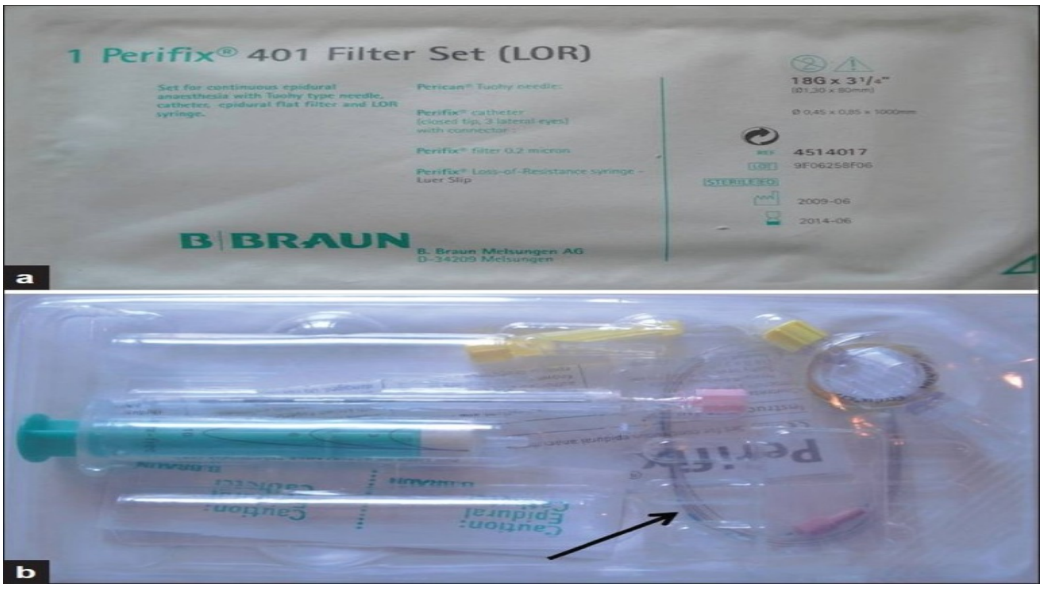


Fig. (30) :- epidural set (Perifix. B. BRAUN Melsungen AG*)*

-

Fig. (31) : GE LOGIQ P5 ultrasound machine

Technique:

A-Technique of US guided continuous intercostal nerve block:

After cleaning the skin with an antiseptic solution, an ultrasound transmission gel is applied to the skin along the lateral edge of the erector spinae muscle.

An ultrasound probe was placed in contact with the skin about 7-8cm from the midline.

The probe is gently manipulated up and down along the axis over a distance of 1-2cm, until intercostal arterial flow became audible as a pulsatile pumping sound.

The position of maximal signal intensity is marked.

1-2ml of dilute local anesthetic is infiltrated subcutaneously at each planned injection site.

The epidural needle is inserted aseptically at this site with its point angled slightly cephalad to make contact with rib at within 1cm in most patients.

While obtaining the same angle of insertion, the needle is walked off the inferior border of the rib.

Then the needle is advanced 3mm below the inferior margin of the rib, with the goal of placing the tip in the space containing the neurovascular bundle (between the internal and innermost intercostal muscles) then the catheter is introduced and secured.

The process is repeated for the remaining levels of blockade.

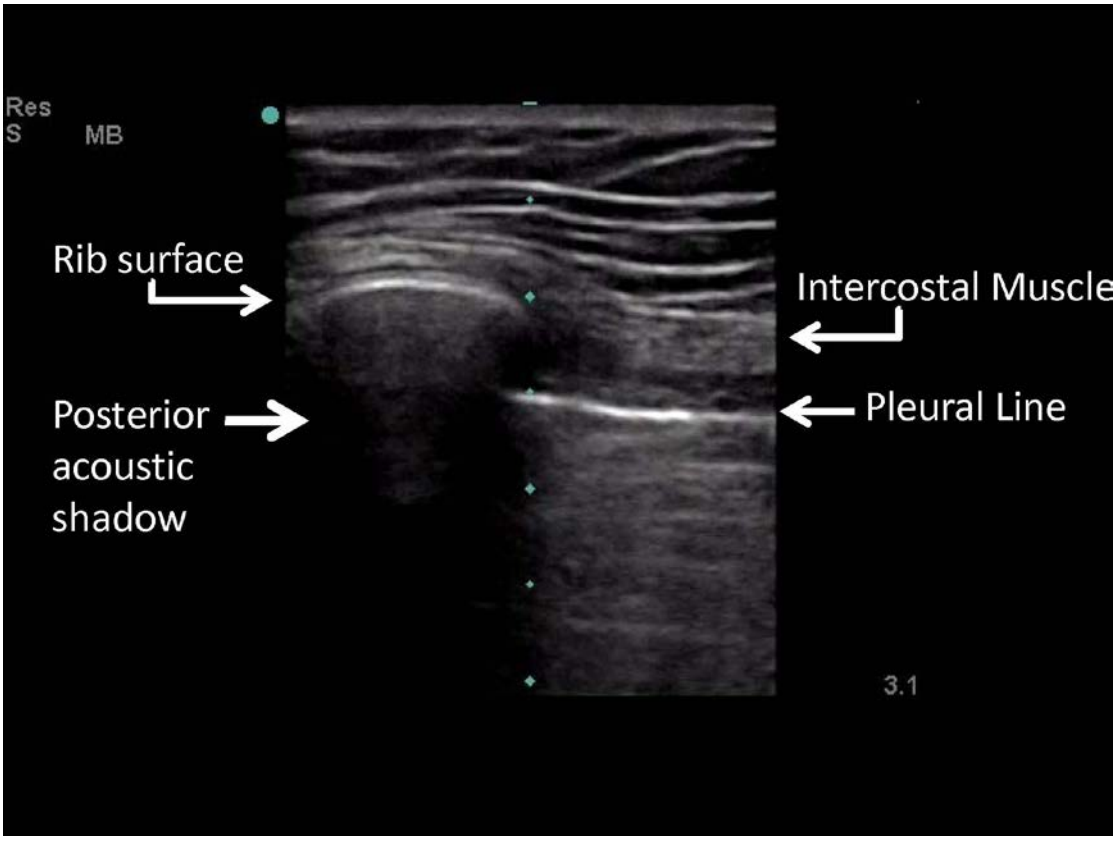


Fig. (32): Ultrasound image of Intercostal space showing pleural line, intercostal muscle and rib surface.

B- Technique of US guided continuous thoracic paravertebral nerve block:

Patient position:

The patient is positioned in lateral decubitus position. This practice precludes the need for special patient positioning or premedication for the block placement.

In addition, the risk of pneumothorax is non existent because the patient already have a chest tube inserted. However, the ability to clearly visualize spinous processes is of crucial importance.

Landmarks:

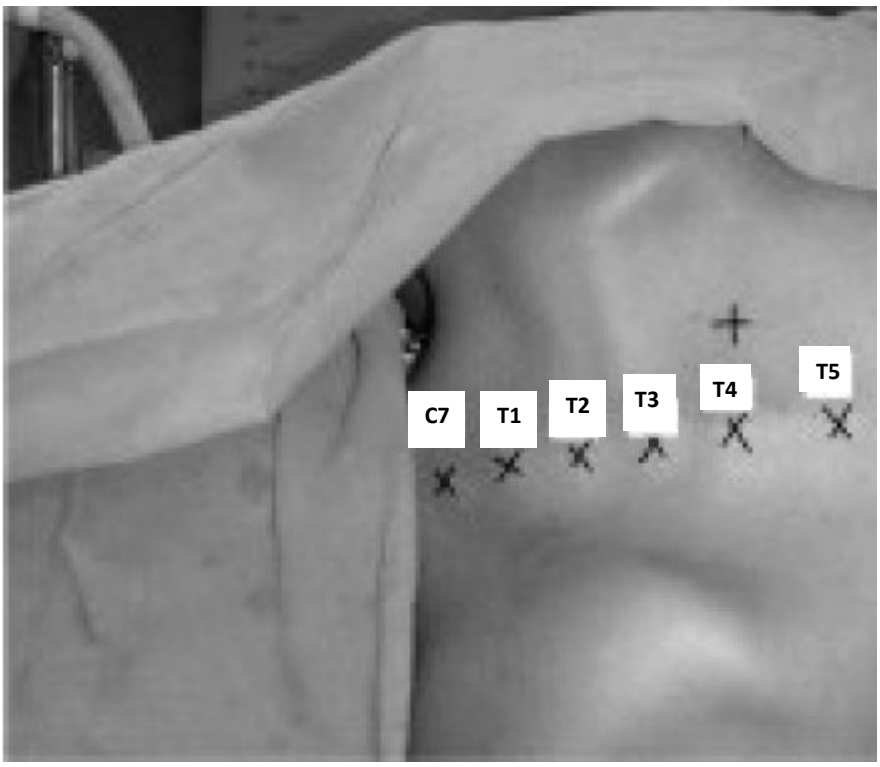
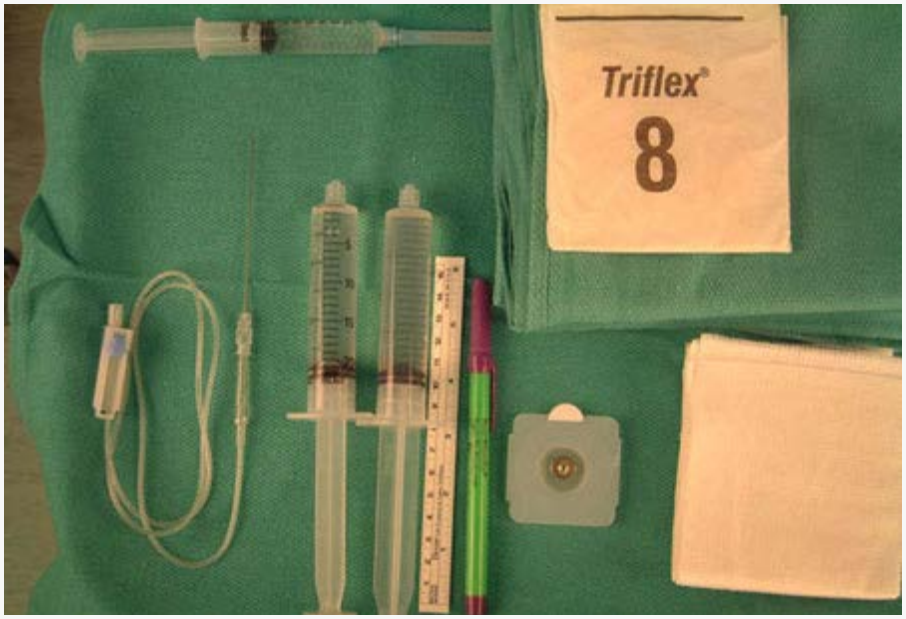


Fig.(33) Landmarks for TPVB lateral position

The landmarks for continuous paravertebral block are identical to those in the single shot technique:

- Initial identification of C7 (the most prominent cervical spine)
- Counting below C7 till the level of the lower border of scapula (T7).
- Identification of T3 and T6 paravertebral region at the surgical side will be performed.
- Midline (spinous processes).
- Paramedial line (2.5cm lateral to spinous processes).
- -For continuous paravertebral blockade, the catheter is ideally inserted 1-2 segmental levels below the thoracotomy incision line.

Equipments:



(Fig. 34): Equipments used for the block.

A standard regional anesthesia tray is prepared with the following equipments:

- Sterile towels and 4″x4″ gauze packs.
- 20-mL syringe with local anesthetic.
- Sterile gloves, marking pen, and surface electrode.
- One 1½” 25-gauge needle for skin infiltration.
- An 18 gauge 8cm epidural needle *(Perifix. B. BRAUN Melsungen AG).*
- GE LOGIQ P5 ultrasound machine.

After surgical disinfection of both cervical and thoracic paravertebral areas an ultrasound transmission gel is applied to the skin.

With the transducer positioned just lateral to the spinous process initial ultrasound investigation of the T3 and T6 paravertebral region at the surgical side will be performed.

Once the transverse processes and ribs are identified, the transducer is moved slightly caudal into the intercostal space between adjacent ribs to identify the thoracic paravertebral space and the adjoining intercostal space.

The tip of the needle will be advanced under direct vision to puncture the costotransverse ligament. Saline (3ml) will then injected deep to the superior costotransverse ligament to demonstrate the position of injectate deep to the ligament.

The catheter is then secured. The catheter should be carefully checked for air CSF, and blood before starting the continuous infusion.

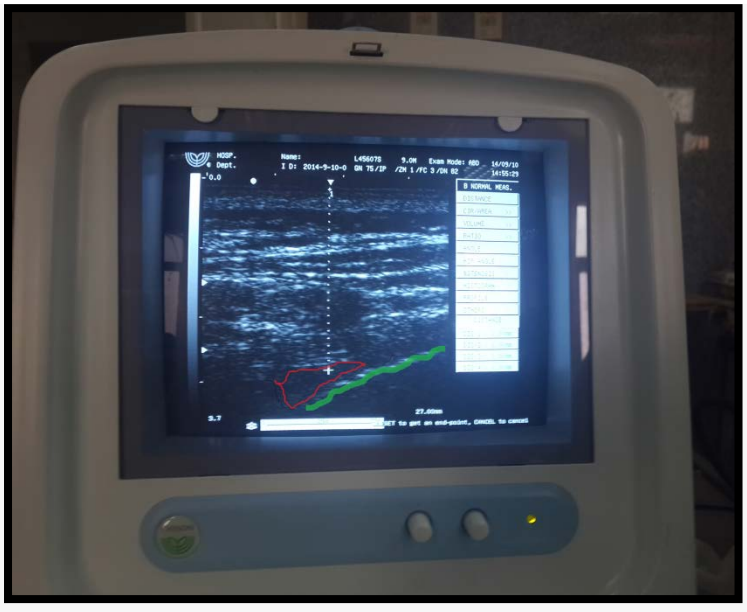


Fig. (35): Ultrasound image of TPVS, green line showing pleura, red line TPVS.

Intercostal nerve block:

-Group Ia:

Will receive 15 ml of bupivacaine 0.5% followed by bupivacaine 0.25% at a rate of 0.1 ml/kg/6hrs for 24 hours.

-Group Ib:

Will receive 15 ml of (bupivacaine 0.5%+1microgram/kg dexmedetomidine) followed by (bupivacaine 0.25% + 1 microgram/kg dexmedetomidine) at a rate of 0.1 ml/kg/6hrs for 24 hours.

Thoracic paravertebral block:

-Group IIa:

Will receive 15 ml of bupivacaine 0.5% followed by bupivacaine 0.25% at a rate of 0.1 ml/kg/6hrs for 24 hours.

-Group IIb:

Will receive 15 ml of (bupivacaine 0.5%+1microgram/kg dexmedetomidine) followed by (bupivacaine 0.25% + 1 microgram/kg dexmedetomidine) at a rate of 0.1 ml/kg/6hrs for 24 hours.

At the end of the operation:-

Reversal of neuromuscular block with neostigmine 0.04-0.08 mg/kg and atropine 0.01- 0.02 mg/kg . When sufficient spontaneous breathing was established and the patient responded adequately to instructions, the trachea was extubated after gentle oropharyngeal suction. After emerging from anesthesia, the patients was transferred to the post anesthesia care unit (PACU) for a 2 hours observation period where the blocks were started after the patient was fully recovered and hemodynamically stable and the following parameters will be measured on admission to PACU, 2h, 4h, 8h, 12h, 24h after surgery:

1. Visual analogue score (VAS) pain at coughing, scale from zero (no pain) to ten (unbearable pain).
2. Pain rescue-analgesia consumption. (rescue analgesia will be administered in the form of morphine 5mg if VAS score is more than 5).
3. Arterial blood pressure and heart rate.
4. Respiratory rate, arterial oxygen saturation (SaO2).
5. Arterial blood gases.
6. FEV1, PEFR, FVC at deep breathing (cough).
7. Blood cortisol levels preoperative, 10 minutes after start of block and 4 hours after extubation.

Statistical analysis:

Analysis of data was done by using SPSS (statistical program for social science version 16) as follows:

- Qualitative data were presented as numbers and percentages.
- Quantitative data were presented as mean ± standard deviation.
- Qualitative data were analysed by using Chi-square test.
- Quantitative data were analysed by using one way ANOVA test.
- Significant data by one way ANOVA test were further analysed by post-hoc analysis (Bonferroni correction) for detection of significant group.
- $P < 0.05$ was considered significant.
- $P < 0.01$ was considered highly significant.
- $P > 0.05$ was considered insignificant.

Results

The study was conducted to best protocol of approved by the institutional ethical committee from January 2016 – October 2017 at Benha University hospitals.

Sixty patients of ASA I, II performing lobectomy were divided into two equal groups which were divided also into another two subgroups. The patient demographic data (age, weight, BMI and time of surgery in min) were compared as shown in table (5).

Table (5): Demographic data and clinical characteristics of the studied **groups.**

Variables	Group Ia N=15	Group Ib N=15	Group 2a N=15	Group 2b N=15	F test (between groups)	Significance	F test	P-value
Age/years Mean ±SD Range	29.07±5.457 P=.407 20-60	30.60±5.742 P=.407 20-60	31.80 ±7.193 P=.804 20-60	28.53 ±5.317 P=.804 20-60	(gr1a,1b) =1.164 (gr2a,2b)= .589 (gr1a,2b)= .471 (gr2a,2b)= 1.164 (gr1a,2a)=1.37465	(gr 1a,1b)=.509 (gr2a,2b)= 775 (gr 1a,2b)=.838 (gr2a,2b)= .551 (gr1a,2a)=0.250894	0.927729598 F crit=2.769430949	0.433437 p>0.05
ASA Mean ±SD Rang	1.27 ±.458 p=..008 I - II	1.27 ±.458 p=..008 I - II	1.40±.507 I - II	1.27±.458 I – II	(gr1a,2b)=1.981 (gr2a,2b)= .459 (gr1a,2b)=1.981 (gr1a,1b)=9.984 (gr1a,2a)=0.571429	(gr1a,2b)=.510 (gr2a,2b)=.510 (gr1a,2b)=.183 (gr1a,1b)= .008 (gr1a,2a)=0.456005	0.301075269 F crit=2.769430949	0.824475 p>0.05
Weight Mean ±SD Range	73.00±7.910 P=.767	71.60±6.916 P=.767	70.40±7.529 P=.045	73.27±5.958 P=.045	(gr1a,1b)=7.133 (gr2a,2b)=4.921 (gr1a,2b)= .546 (gr1a,2a)=0.850264 (gr 2a,1b)=0.20667	(gr1a,1b)=.129 (gr2a,2b)=.181 (gr1a,2b)= .798 (gr1a,2a)=0.364355 (gr2a,1b)=0.652895	0.523905787	0.667632 p>0.05
BMI Mean ±SD Range	27.48±2.162 18.5 -30 kg m^2 p=.766 24-32	27.13±1.939 18.5 -30 kg m^2 p=.766 24-30	26.27±2.013 18.5 -30 kg m^2 P=.238 22-29	26.84±1.838 18.5 -30 kg m^2 P=.238 24-30	(gr1a,1b)= .494 (gr2a,2b)= 1.437 (gr2a,2b)=1.437 (gr1a,1b)=.336 (gr1a,2a)=1.918612	(gr1a,1b)=.831 (gr2a,1b)= .388 (gr2a,2b)=.388 (gr1a,2b)= .926 (gr1a,2a)=0.176947	0.801937	0.498049 p>0.05
Time of surgery in min Mean ±SD Range	113.33 ±14.475 P=.366 90-140	118.00±13.732 P=.366 100-140	116.33±13.25 P=.350 100-140	119.67±13.689 P=.350 100-140	(gr1a,1b)=.747 (gr2a,2b)=2.445 (gr2a,1b)=.714 (gr1a,2b)= 2.272 (gr1a,2a)=0.346365	(gr1a,1b)=..582 (gr2a,2b)= .115 (gr2a,1b)=. .601 (gr1a,2b)=.135 (gr1a,2a)=0.560896	0.57172471 F crit =2.769430949	0.635963 p>0.05

- Data are presented as number; shown as mean±SD, numbers and ranges.

This table shows that the four groups were matched as regard age, ASA, Weight ,BMI, Time of surgery and the difference was statistically non significant (p>0.05).

Visual analogue pain score (VAS):

Also the VAS score were compared at PACU admission, 2h, 4h, 8h, 12h and at 24h as shown in table (6).

Table(6): Mean visual analogue scale (VAS) on coughing among the studied groups.

Variables	Group Ia N=15	Group Ib N=15	Group 2a N=15	Group 2b N=15	F test (between groups)	Significance	F test	P-value
VAS PACU Mean ±SD Range	5.47±990 P=.316 4-7	5.40±.986 P=.316 4-7	5.40±.910 P=.427 4-7	5.47±.990 P=.427 4-7	(gr1a,1b)=1.010 (gr2a,2b)= 2.877 (gr2a,1b)= .177 (gr1a,2b)= .501 (gr1a,2a)=0.036842	(gr1a,1b)= .425 (gr2a,2b)= . (gr2a,1b)= .910 (gr1a,2b)= .689 (gr1a,2a)=0.849172	0.023629 F crit=2.769430949	0.995026031 p>0.05
VAS2h Mean ±SD Range	3.40±.507 3-4	2.13±.352 2-3	2.00±.000 2-2	1.00±.000 1-1	(gr 1a,1b)= 3.39 (gr2a,1b)=2.153846 (gr2a,2b)=65535 (gr1a,2b)=336 (gr1a,2a)=114.3333	(gr 1a,1b)=1.17E08 (gr2a,1b)=0.153357 (gr2a,2b)= #NUM! (gr1a,2b)=3.94E17 (gr1a,2a)=2.15E-11	152.6	6.37773E-27 P<0.01
VAS4h Mean ±SD Range	6±.0 6-6	2.733333±0.703732 2-4	2±.000 2-2	1±000 1-1	(gr1a,1b)=323.2115 (gr1b,2a)=2.153846 (gr2a,2b)=(gr1a,2b)= (gr1a,2a)=65535	(gr1a,1b)=6.51E-17 (gr1b,2a)=0.153357 (gr2a,2b)=(gr1a,2b) =(gr1a,2a)=#NUM!	567.5385	7.24E-42 P<0.01
VAS8h Mean ±SD Range	3.93±.458 3-5	2.20±.414 2-3	2.20±414 2-3	1.33±.488 1-2	(gr 1a,1b)=118.3 (gr 1b,2a)=0 (gr 2a,2b)=27.51163 (gr1a.2b)=226.5319 (gr1a,2a)=118.3	(gr 1a,1b)=1.46E-11 (gr 1b,2a)=1 (gr 2a,2b)=1.42E-05 (gr1a,2b)=6E-15 (gr1a,2a)=1.46E-11	90.26908	1.96E-21 P<0.01
VAS12h Mean ±SD Range	5.00±.845 4-6	4.27±1.163 6-6	3.53±.516 3-4	2.20±.414 2-3	(gr 1a,1b)= 3.903226 (gr 1b,2a)= 4.982353 (gr 2a,2b)= 60.86957 (gr 1a,2b)= 132.7742 (gr 1a,2a)= 32.8932	(gr 1a,1b)= 0.058124 (gr 1b,2a)= 0.033786 (gr 2a,2b)= 1.69E-08 (gr 1a,2b)= 3.86E-12 (gr 1a,2a)= 3.73995E-06	34.16603295	1.09586E-12 P<0.01

VAS24h Mean ±SD Range	**5.40±.828**	**3.60±.507**	**2.53±.516**	**1.27±.458 1-2**	**(gr 1a,1b)= 51.54545 (gr 1b,2a)= 32.58182 (gr 1a,2b)= 286.2553 (gr 2a,2b)= 50.54 (gr 1a,2a)= 129.43**	**(gr 1a,1b)= . 8.18E-08 (gr 1b,2a)= 4.03E-06 (gr 1a,2b)= 3.1E-16 (gr 2a,2b)= 9.81E-08 (gr 1a,2a)= 5.19E-12**	**129.4138702**	**3.7113E-25 P<0.01**

Data are presented as number; shown as mean± SD, numbers and ranges.

This table shows that VAS at PACU admission was non statistically significant difference ($p>0.05$) while a highly statistically significant ($p<0.01$) difference between the four groups regarding VAS score on coughing recorded at 2, 4, 8, 12, 24 hours. After comparisons between four groups group 2b was the best group showing the lowest pain score which has high significance between four groups while group1a the group which showed the highest pain scores with low significance between four groups.

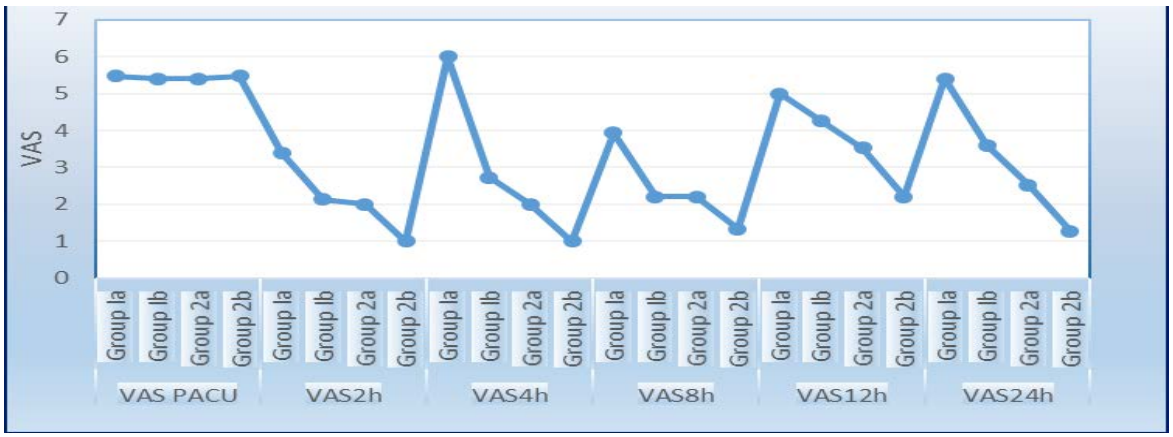


Fig. (36) Mean of VAS of studied groups

Pain rescue analgesia (PRA)

Also the PRA was compared at PACU admission, 2h, 4h, 8h, 12h and at 24h as shown in table (7).

Table (7): Mean of PRA among the studied groups (morphine in mg)

Variables	Group Ia N=15	Group Ib N=15	Group 2a N=15	Group 2b N=15	F test (between groups)	Significance	F test	P-value
PRA PACU Mean ±SD Range	1.53±.516 1-1	1.47±.516 1-2	1.53±.56 1-2	1.53±.516 1-2	(gr1a,1b)=.522 (gr1a,2a)= .522 (gr2a,1b))=.522 (gr1a,2b)=.522 (gr2a,2b)= 1.33E-14	(gr1a,1b)= .483 (gr1a,2a)= .483 (gr1a,2b)=.483 (gr2a,1b)=.483 (gr2a,2b)= 1	0.0625 F crit = 2.769430949	0.979369634 p>0.05
PRA 2h Mean ±SD Range	2.6±0.5079 2-3	1.866±0.356 1-2	2±000 2-2	1±000 1-1	(gr1a,1b)= 21.175 (gr1a,2a)= 22.90909 (gr1a,2b)= 22.909091 (gr2a,1b)= 4.3076928 (gr2a,2b)= 9.9647052	(gr1a,1b)= 8.24E-05 (gr1a,2a)= 4.97E-05 (gr1a,2b)= 4.97384E-05 (gr2a,1b)= 0.047241244 (gr2a,2b)= 0.003798572	68.6	9.5E-19 P<0.01
PRA 4h Mean ±SD Range	2.06666± 0.258192-3	2.1333± 0.83380 1-3	2.1333± 0.35186 2-3	1.26666± 0.703731 -3	(gr1a,1b)=0.0875 (gr1a,2a)=0.35 (gr1a,2b)=17.0845 (gr2a,2b)= 18.2 (gr2a,1b)=-8.7E-15	(gr1a,1b)= 0.769562 (gr1a,2a)= 0.55886 (gr1a,2b)= 0.000294 (gr2a,2b)= 0.000205 (gr2a,1b)=#NUM!	7.788505747	0.000196242 P<0.01
PRA 8h Mean ±SD Range	2.1333± 0.351862-3	2.2± 0.41403 2-3	2.2± 0.41403 2-3	1.33333± 0.487950 1-2	(gr1a,1b)= 0.225806 (gr1a,2b)= 26.52632 (gr2a,1b)= 0 (gr2a,2b)= 27.51163 (gr1a,2a)= 0.225806	(gr1a,1b)=0.638337 (gr1a,2b)= 1.84E-05 (gr2a,1b)= 1 (gr2a,2b)= 1.42E-05 (gr1a,2a)=0.638337	15.26126126	2.24623E-07 P<0.01
PRA 12h Mean ±SD Range	5±0.845154 4-6	4.266667± 1.162919 3-6	3.533333±. 0.516398 3-4	2.2 ± 0.414039 2-3	(gr1a,1b)= 3.903225806 (gr2a,1b)= 4.982353 (gr1a,2b)= 132.7742 (gr2a,2B)= 60.86957 (gr1a,2a)=32.8932	(gr1a,1b)= 0.058124 (gr2a,1B)= 0.033786 (gr1a,2b)= 3.86E-12 (gr2a,2b)= 1.69E-08 (gr1a,2a)=3.74E-06	34.16603295	1.09586E-12 P<0.01

PRA 24h Mean ±SD Range	**5.4±0.828078671 4-6**	**1.33±.488 3-4**	**2.533±0.516397779 2-3**	**1.2667 ±.0.4577377708 1-2**	**(gr1a,1b)= 51.54545 (gr2a,1b)= 32.58182 (gr1a,2b)= 286.2553 (gr2a,2b)= 50.54 (gr1a,2a)=129.43**	**(gr1a,1b)= 8.18E-08 (gr2a,1b)= 4.03E-06 (gr1a,2b)= 3.1E-16 (gr2a,2b)= 9.81E-08 (gr1a,2a)=5.19E-12**	**129.4139**	**3.71E-25 P<0.01**

Data are presented as number; shown as mean± SD, numbers and ranges. 5 mg=2 no=1

This table shows that PRA at PACU admission was statistically non-significant (p>0.05) while a highly statistically significant (p<0.01) difference between the four groups regarding PRA 2h,4h,8h,12h,24h, after comparisons between four groups group 2b was the best group which showed the least PRA consumption which has high significance between four groups while group1a the group which showed the highest PRA consumption and has low significance between four groups.

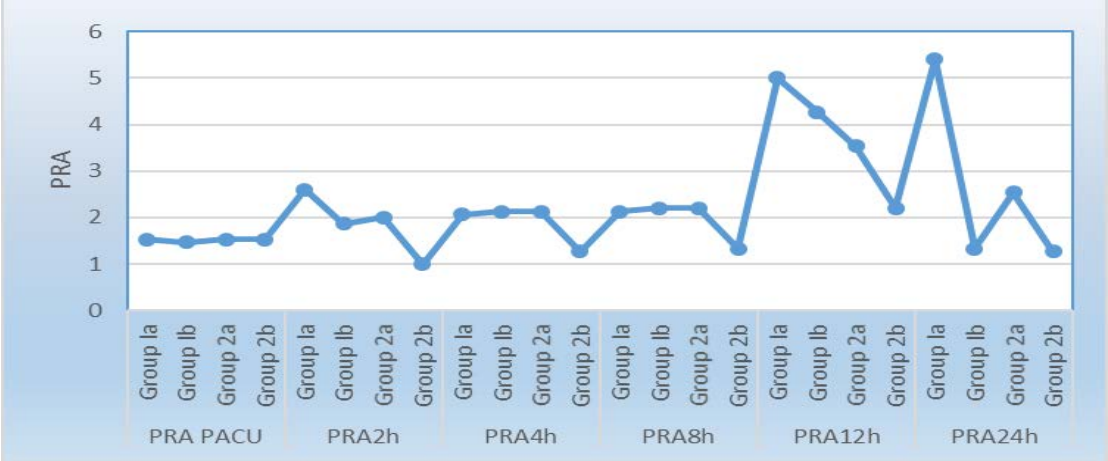


Fig. (37) Mean of PRA of studied groups

Mean arterial pressure (MAP; mmHg)

Also the MAP was compared at PACU admission, 2h, 4h, 8h, 12h and at 24h as shown in table (8).

Table (8): Mean of Arterial blood pressure (MAP) among the studied groups.

Variables	Group Ia N=15	Group Ib N=15	Group 2a N=15	Group 2b N=15	F test (between groups)	Significance	F test	P-value
MAPPACU Mean ±SD Range	108.7333 ±6.734418 90-120	103.9333 ±8.672342 90-120	109.7333 ± 4.697517 103-116	102.9333 ±9.764854 90-120	(gr1a,1b)=2.866577 (gr1b,2a)=5.187292 (gr2a,2b)=5.907048 (gr1a,2b)=3.586233 (gr1a,2a)=0.222489	(gr1a,1b)=0.101536 (gr1b,2a)=0.030588 (gr2a,2b)=0.021741 (gr1a,2b)=0.068635 (gr1a,2a)=0.640805	2.911157356 Fcrit= 2.769430949	0.042301952 P<0.05
MAP2h Mean ±SD Range	86.00±9.032 76-96	86.00±7.069 63-83	77.73±8.040 68-90	67.93±13.869 53-90	(gr1a,1b)= 27.75065161 (gr1b,2a)= 7.038391225 (gr2a,2b)= 5.605655203 (gr1a,2b)= 17.87382658 (gr1a,2a)=7.010943	(gr1a,1b)= 1.33376E-05 (gr1b,2a)= 0.012995618 (gr2a,2b)= 0.025046248 (gr1a,2b)= 0.000227534 (gr1a,2a)=0.013155	10.21797072	1.82147E-05 P<0.01
MAP4h Mean ±SD Range	105.67±3.395 100-110	76.33±11.493 61-93	83.13333 ± 7.744737 72-96	70.06667 ± 4.3337 62-76	(gr1a,1b)= 89.86737 (gr1b,2a)= 3.611067 (gr2a,2b)= 32.51657 (gr1a,2b)= 627.3074 (gr1a,2a)= 106.5141	(gr1a,1b)= 3.09E-10 (gr1b,2a)=0.067738 (gr2a,2b)= 4.09E-06 (gr1a,2b)=1.03E-20 (gr1a,2a)=4.77E-11	65.01916	3.05E-18 P<0.01
MAP8h Mean ±SD Range	86.27±5.418 80-98	72.87±3.399 66-80	74.60±3.979 70-80	70.40±5.974 60-80	(gr1a,1b)= 65.84563 (gr1b,2a)= 1.645913 (gr2a,2b)= 5.136439 (gr1a,2b)= 58.06238 (gr1a,2a)= 45.18866	(gr1a,1b)= 7.8E-09 (gr1b,2a)= 0.210034 (gr1a,2b)= 2.67E-08 (gr2a,2b)= 0.031349 (gr1a,2a)=2.68E-07	32.1444078	3.23353E-12 P<0.01
MAP12h Mean ±SD Range	96.53±7.596 86-110	89.47±7.396 80-103	82.13±9.357 66-93	78.13±11.581 53-100	(gr1a,1b)= 6.664859 (gr1b,2a)= 6.05591 (gr2a,2b)= 114.2218 (gr1a,2b)= 183.4027 (gr1a,2a)29.83119	(gr1a,1b)= 0.01536 (gr1b,2a)= 0.020288 (gr2a,2b)= 2.17E-11 (gr1a,2b)= 8.16E-14 (gr1a,2a)=7.86E-06	76.72437	7.94E-20 P<0.01

MAP24h Mean ±SD Range	**102.40±7.366**	**85.33±5.205**	**77.53±8.210 63-93**	**74.13±6.334**	**(gr1a,1b)= 53.70546 (gr1b,2a)= 9.656656 (gr1a,2b)= 194.7726 (gr2a,2b)= 7.066845 (gr1a,2a)=76.23507**	**(gr1a,1b)= 5.59E-08 (gr1b,2a)= 0.004298 (gr1a,2b)= 3.91E-14 (gr2a,2b)= 0.012833 (gr1a,2a)=1.76E-09**	**64.59174**	**3.52E-18 P<0.01**

Data are presented as mean± SD

This table shows a highly statistically significant($p<0.01$) difference between the four groups regarding MAP recorded at MAP at PACU admission ,2h, 4h, 8h, 12h and at 24h of studied groups. After comparisons between four groups group 2b was low significant between four groups which showed the lowest MAP while group1a has high significance between four groups which showed highest MAP.

Fig. (38) Mean of MAP of studied groups

Heart rate (HR; beats/min)

Also the HR was compared at PACU admission, 2h, 4h, 8h, 12h and at 24h as shown in table (9).

Table (9): Mean HR measurements of patients Heart Rate (HR) (beats/min) among the studied groups.

Variables	Group Ia N=15	Group Ib N=15	Group 2a N=15	Group 2b N=15	F test (between groups)	Significance	F test	P-value
HR PACU Mean ±SD Range	138.27±4.803 130-145	146.40±7.385 135-157	141.53±7.754 130-159	132.93±4.589 125-140	(gr1a,1b)= 12.78537 (gr1b,2a)= 3.098256 (gr2a,2b)= 13.66416 (gr1a,2b)= 9.667674 (gr1a,2a)=1.924098	(gr1a,1b)= 0.001294 (gr1b,2a)= 0.089298 (gr2a,2b)= 0.000942 (gr1a,2b)= 0.004279 (gr1a,2a)=0.176349	12.09894 Fcrit= 2.769430949	3.27E-06 P<0.01
HR 2h Mean ±SD Range	116.27±5.725 110-130	104.667±3.1773 100-110	111.53±6.28 100-120	103.80±8.117 95-117	(gr1a,1b)= 47.07508 (gr1b,2a)= 14.24573 (gr2a,2b)= 8.507994 (gr1a,2b)= 23.6277 (gr1a,2a)= 4.646083	(gr1a,1b)= 1.87E-07 (gr1b,2a)= 0.000767 (gr2a,2b)= 0.006893 (gr1a,2b)= 4.06E-05 (gr1a,2a)= 0.039868	14.16212	5.54E-07 P<0.01
HR4h Mean ±SD Range	127.13±5.303 115-135	119.80±12.061 105-140	118.80±6.581 100-127	111.60±9.249 100-124	(gr1a,1b)= 4.647207 (gr1b,2a)= 0.079461178 (gr2a,2b)= 6.03459 (gr1a,2b)= 31.84105572 (gr1a,2a)= 14.58139	(gr1a,1b)= 0.039846 (gr1b,2a)= 0.780101974 (gr2a,2b)= 0.020489 (gr1a,2b)= 4.80566E-06 (gr1a,2a)= 0.000682	8.01133644	0.000156549 P<0.01
HR8h Mean ±SD Range	102.73±3.494 100-110	98.26667 ± 5.787507 90-107	105.6 ± 6.333584 100-118	93.73333 ± 3.217512 89-98	(gr1a,1b)= 6.547822 (gr1B,2a)= 10.95873 (gr2a,2b)= 41.85469 (gr1a,2b)= 53.85184 (gr1a,2a)=2.355843	(gr1a,1b)= 0.016194 (gr1B,2a)= 0.002571 (gr2a,2b)= 5.22E-07 (gr1a,2b)= 5.44E-08 (gr1a,2a)=0.136038	16.86133	6.34E-08 P<0.01
HR12h Mean ±SD Range	113.40±5.096 100-120	105.27±7.860 95-120	110.80±8.962 100-130	96.33333 ± 3.287784 90-102	(gr1a,1b)= 11.30758 (gr1b,2a)= 3.232105 (gr2a,2b)= 34.45056 (gr1a,2b)= 118.7861 (gr1a.2a)= 0.954032	(gr1a,1b)= 0.002249 (gr1b,2a)= 0.083 (gr2a,2b)= 2.6E-06 (gr1a,2b)= 1.39E-11 (gr1a.2a)= 0.337059	19.11626	1.17E-08 P<0.01

HR24h Mean ±SD Range	**115.3333 ± 3.538899 110-120**	**102± 5.8064 90-110**	**107.07±5.418 100-118**	**100.73±8.102 90-115**	**(gr1a,1b)= 57.6725 (gr1b,2a)= 6.105708 (gr2a,2b)= 6.333968 (gr1a,2b)= 40.9074 (gr1a.2a)=24.47851**	**(gr1a,1b)= 2.84E-08 (gr1b,2a)= 0.019826 (gr2a,2b)= 0.017851 (gr1a,2b)= 6.35E-07 (gr1a.2a)=3.2E-05**	**18.64574**	**1.65E-08 P<0.01**

Data are presented as mean± SD and ranges.

This table shows highly statistically significant (p<0.01) difference between the four groups regarding HR recorded at PACU admission, 2, 4, 8,12 and at 24hr . While HR nearly the same among patients of the four groups, after comparisons between four groups group 2b was the group of high significance which showed the lowest while group1a was the group of low significance between four groups which showed the highest HR.

Fig. (39) Mean of HR of studied groups

Respiratory rate (RR)

Also the RR was compared at PACU admission, 2h, 4h, 8h, 12h and at 24h as shown in table (10).

Table (10): Mean of respiratory rate (RR) (breath/min) among the studied groups.

Variables	Group Ia N=15	Group Ib N=15	Group 2a N=15	Group 2b N=15	F test (between groups)	Significance	F test	P-value
RR PACU Mean±SD Range	27.4 ± 2.164651 24-31	26.4 ± 2.585675 23-31	28.93333 ± 3.011091 23-33	30.86667 ± 4.911599 24-40	(gr1a,1b)= 1.68924 (gr1b,2a)= 6.25719 (gr2a,2b)= 1.319095 (gr1a,2b)= 6.111245 (gr1a.2a)= 2.564404	(gr1a,1b)= 0.2043 (gr1B,2a)= 0.01849 (gr2a,2b)= 0.260472 (gr1a,2b)= 0.019775 (gr1a.2a)= 0.120517	1.760044 Fcrit=2.7694309	0.16531 (p>0.05)
RR 2h Mea±SD Range	19.40±3.680 14-25	15.60±2.414 12-18	18.80±2.808 16-24	16.00±1.852 14-18	(gr1a,1b)= 11.18142 (gr1b,2a)= 11.2 (gr2a,2b)= 10.39394 (gr1a,2b)= 10.21717 (gr1a.2a)= 0.252	(gr1a,1b)=0.00236 (gr1b,2a)= 0.002343 (gr2a,2b)= 0.003205 (gr1a,2b)= 0.003436 (gr1a.2a)= 0.619595	7.267225326	0.0003351 (p<0.01)
RR4h Mean±SD Range	25.60±3.135055 20-30	19.6±2.028 17-23	22.33333 ±2.319688 19-26	19±1.511858 17-22	(gr1a,1b)= 38.33671 (gr2a,1b)= 11.62747 (gr1a,2b)= 53.93632 (gr2a,2b)= 21.73913 (gr1a.2a)= 10.52411	(gr1a,1b)=1.09E-06 (gr1b,2a)=0.001991 (gr1a,2b)=5.37E-08 (gr2a,2b)=6.98E-05 (gr1a.2a)= 0.003045	25.09457	2.02E-10 (p<0.01)
RR8h Mean±SD Range	21.20±3.840 18-28	15.20±1.014 14-16	19.20±2.111 16-22	15.60±.828 14-16	(gr1a,1b)= 34.23913 (gr1b,2a)= 43.75 (gr2a,2b)= 37.8 (gr1a,2b)= 30.48889 (gr1a.2a)= 3.125	(gr1a,1b)= 2.73E-06 (gr1b,2a)= 3.56E-07 (gr2a,2b)= 1.23E-06 (gr1a,2b)= 6.68E-06 (gr1a.2a)= 0.087997	24.02185792	4.02E-10 (p<0.01)

RR12h Mean±SD Range	**24.66667 ± 3.373567 20-31**	**20.86667 ± 2.294922 17-24**	**22.73333 ± 1.830951 20-26**	**18.06667 ± 2.313521 15-22**	**(gr1a,1b)= 13.01087 (gr1b,2a)= 6.064088 (gr2a,2b)= 37.52735 (gr1a,2b)= 39.04781 (gr1a.2a)= 3.80543**	**(gr1a,1b)= 0.001192 (gr1b,2a)= 0.020211 (gr2a,2b)= 1.3E-06 (gr1a,2b)= 9.39E-07 (gr1a.2a)= 0.06116**	**18.70436**	**1.58E-08 (p<0.01)**
RR24h Mean±SD Range	**23.40±6.057 20-35**	**17.20±2.111 14-20**	**19.60±.828 18-20**	**14.00±.000 14-14**	**(gr1a,1b)= 14.01458 (gr1B,2a)= 16.8 (gr2a,2b)= 686 (gr1a,2b)= 36.1285 (gr1a.2a)= 5.795872**	**(gr1a,1b)= 0.000832 (gr1B,2a)= 0.000322 (gr2a,2b)= 3.1E-21 (gr1a,2b)= 1.78E-06 (gr1a.2a)= 0.022901**	**22.54439891**	**1.06256E-09 (p<0.01)**

Data are presented as number; shown as mean± SD, numbers and ranges.

This table shows that RR at PACU admission was non statistically significant different (p>0.05) while RR recorded at 2h, 4, 8, 12 and at 24 hr was a highly statistically significant difference (p<0.01), after comparisons between four groups group 2b was the group of high significance which showed the lowest RR while group1a the group of low significance between four groups which showed the highest RR.

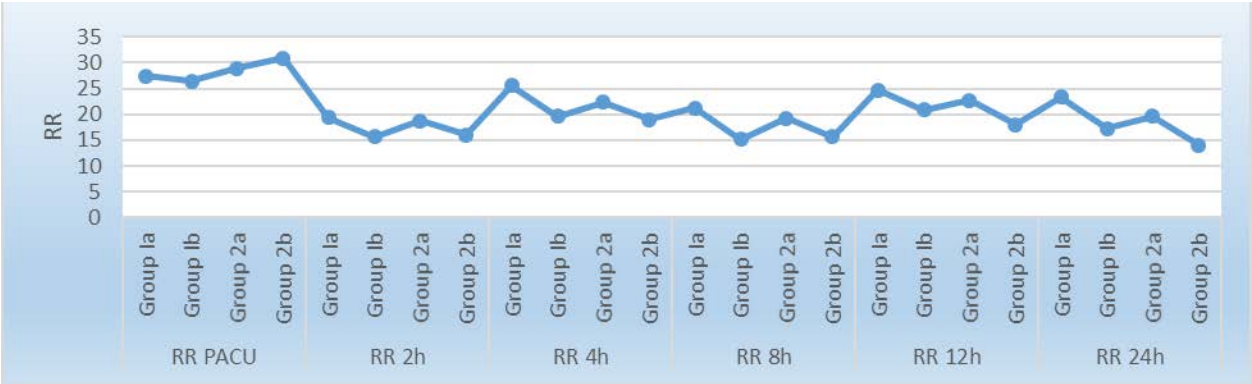


Fig. (40) Mean of RR of studied groups

Oxygen Saturation (SPO2)

Also the RR was compared at PACU admission, 2h, 4h, 8h, 12h and at 24h as shown in table (11).

Table (11): mean of Oxygen Saturation (SaO2) among the studied groups.

Variables	Group Ia N=15	Group Ib N=15	Group 2a N=15	Group 2b N=15	F test (between groups)	Significance	F test	P-value
SaO2 PACU Mean ±SD Range	98.02667 ±. 0.579984 97.2-99.3	98.70667 ± 0.881935 97.2-99.7	98.13333 ± 0.509435 97.2-99	98.35333 ± 0.492612 97.7-99.2	(gr1a,1b)= 6.225147 (gr1b,2a)= 4.753213 (gr2a,2b)= 1.445667 (gr1a,2b)= 2.764309 (gr1a,2a)= 0.286399	(gr1a,1b)= 0.018764 (gr1b,2a)= 0.037808 (gr2a,2b)= 0.239294 (gr1a,2b)= 0.107544 (gr1a,2a)= 0.596762	0.780466 F =2.769430949	0.509838 (p>0.05)
SaO2 2h Mean ±SD Range	97.37333 ± 0.349421 96.8-97.9	98.10667 ± 0.373146 97.5-98.9	97.93333 ±0.361873 97.2-99	98.26667 ±0.355903 97.6-98.8	(gr1a,1b)= 30.86735 gr1b,2a)= 1.667959 (gr2a,2b)= 6.469501 (gr1a,2b)= 48.12098 (gr1a,2a)= 18.58939	(gr1a,1b)= 6.09E-06 (gr1b,2a)= 0.207092 (gr2a,2b)= 0.016781 (gr1a,2b)= 1.53E-07 (gr1a,2a)= 0.000181	17.4985	3.89E-08 (p<0.01)
SaO24h Mean ±SD Range	97.4133 ±0.287518 96.9-97.9	97.7933 ±0.359497-98.3	97.67333 ±0.446361 96.8-98.3	97.98667 ±0.385202 97.1-98.5	(gr1a,1b)= 10.22157 gr1b,2a)= 0.657582 (gr2a,2b)= 4.236438 (gr1a,2b)= 21.34048 (gr1a,2a)= 3.596959	(gr1a,1b)= 0.00343 (gr1b,2a)= 0.424254 (gr2a,2b)= 0.04898 (gr1a,2b)= 7.84E-05 (gr1a,2a)= 0.068246	6.171915	0.001064 (p<0.01)
SaO28h Mean ±SD Range	97.01333 ±0.51251 96-97.5	97.67333 ±0.48912 96.8-98.3	97.54667 ± 0.568038 96.3-98.3	97.98667 ±0.313657 97.5-98.4	(gr1a,1b)= 13.01841 (gr1b,2a)= 0.428305 (gr2a,2b)= 6.897082 (gr1a,2b)= 39.35954 (gr1a,2a)= 7.289294	(gr1a,1b)= 0.001189 (gr1b,2a)= 0.518162 (gr2a,2b)= 0.01384 (gr1a,2b)= 8.79E-07 (gr1a,2a)=0.011632	10.70068	1.16E-05 (p<0.01)
SaO212h Mean ±SD Range	96.34 ±0.785403 94.1-97.3	97.05333 ±0.667476 96-97.8	97.38 ±0.578421 96-98	97.98667 ±0.364234 97.2-98.4	(gr1a,1b)= 7.184491 (gr1b,2a)= 2.051886 (gr2a,2b)= 11.81553 (gr1a,2b)= 54.26468 (gr1a,2a)= 17.05225	(gr1a,1b)= 0.012182 (gr1b,2a)= 0.163088 (gr2a,2b)= 0.001855 (gr1a,2b)= 5.07E-08 (gr1a,2a)= 0.000297	18.46153	1.89E-08 (p<0.01)

SaO2 24h Mean ±SD Range	**96.34 ±0.785403 94.1-97.3**	**97.05333 ±0.667476 96-97.8**	**97.38 ±0.578421 96-98**	**97.98667 ±0.364234 97.2-98.4**	**(gr1a,1b)= 7.184491 (gr1b,2a)= 2.051886 (Gr2a,2b)= 11.81553 (gr1a,2b)= 54.26468 (gr1a,2a)= 17.05225**	**(gr1a,1b)= 0.012182 (gr1b,2a)= 0.163088 (Gr2a,2b)= 0.001855 (gr1a,2b)= 5.07E-08 (gr1a,2a)=0.000297**	**18.46153**	**1.89E-08 (p<0.01)**

Data are presented as number; shown as mean±SD, numbers and range.

This table shows that SaO2 at PACU admission was non statistically significant different (p>0.05) while SaO2 recorded at 2,4,8,12 and at 24 hr was highly statistically significant different, After comparisons between four groups group 2b was the group of highest significance between four groups which showed the highest SaO2 while group1a the group of low significance which showed the lowest SaO2 between four groups.

Fig. (41) Mean of SaO2 of studied groups

Arterial blood gases (ABG):

Also the ABG was compared at preoperative, PACU admission, 2h ,4h ,8h ,12h and at 24h as shown in table (12).

Table (12): mean of ABG of the studied groups.

Variables	Group Ia N=15	Group Ib N=15	Group 2a N=15	Group 2b N=15	F test (between groups)	Significance	F test	P-value
ABG preopertive PO2 Mean ±SD Range	72±3.760699 69-79	72.6±3.561701 68-77	71.1±1.325573 69.5-73	71.6±2.131398 70-75	(gr1a,1b)=0.201278 (gr1b,2a)= 2.336795 (gr2a,2b)= 0.595238 (gr1a,2b)= 0.12844 (gr1a,2a)= 0.764151	(gr1a,1b)= 0.657144 (gr1b,2a)= 0.137569 (gr2a,2b)= 0.446863 (gr1a,2b)= 0.722743 (gr1a,2a)= 0.389469	0.728978 F =2.769430949	0.539022 (p>0.05)
ABG preopertive PCO2 Mean ±SD Range	40.06±1.709 38-43	38.6±2.5856 35-42	40.266±2.814 39-44	40.133±3.226 35-45	(gr1a,1b)= 3.35778 (gr1b,2a)= 2.852021 (gr2a,2b)= 0.014545 (gr1a,2b)= 0.005 (gr1a,2a)= 0.055312	(gr1a,1b)= 0.077544 (gr1b,2a)= . 0.102367 (gr2a,2b)= . 0.904866 (gr1a,2b)= 0.944131 (gr1a,2a)=0.815777	1.313792	0.27899 (p>0.05)
ABG Preopertive PH Mean ±SD Range	7.32±0.041404 7.3-7.4	7.3±1.84E-15 7.3-7.3	7.30±0.02582 7.3-7.4	7.30±0.035187 7.3-7.4	(gr1a,1b)=9.8 3.5 (gr1b,2a)=1 (gr2a,2b)= 0.35 (gr1a,2b)=0.225806 (gr1a,2a)=1.12	(gr1a,1b)= 0.071854 (gr1b,2a)= 0.325875 (gr2a,2b)= 0.55886 (gr1a,2b)= 0.638337 (gr1a,2a)=0.298964	1.283333	0.289017 (p>0.05)

ABG PACU PO2 Mean ±SD Range	**78.20±4.601 73-84**	**75.40±3.851 69-80**	**76.40±1.549 75-79**	**77.60±2.746 75-82**	**(gr1a,1b)= 3.266667 (gr1b,2a)= 0.870647 (gr2a,2b)= 2.172414 (gr1a,2b)= 0.18806 (gr1a,2a)= 2.061818**	**(gr1a,1b)= 0.081457 (gr1b,2a)= 0.358753 (gr2a,2b)= 0.151661 (gr1a,2b)= 0.667859 (gr1a,2a)=0.162109**	**2.037313**	**0.119047 (p>0.05)**
ABG PACU PCO2 Mean ±SD Range	**37.1±2.861069 34-41.5**	**34.8±2.210365 32-38**	**36.4±3.680062 30-41**	**35.8±2.396426 33-40**	**(gr1a,1b)= 6.070492 (gr1b,2a)= 2.083721 (gr2a,2b)= 0.28 (gr1a,2b)= 1.82 (gr1a,2a)= 0.338264**	**(gr1a,1b)= 0.020151 (gr1b,2a)= 0.159973 (gr2a,2b)= 0.600872 (gr1a,2b)= 0.188123 (gr1a,2a)= 0.565486**	**1.760044 Fcrit=2.7694309**	**0.16531 (p>0.05)**
ABG PACU PH Mean ±SD Range	**7.31±0.035187 7.3-7.4**	**7.32±0.041404 7.3-7.4**	**7.32±0.041404 7.3-7.4**	**7.32±0.041404 7.3-7.4**	**(gr1a,1b)= 0.225806 (gr1b,2a) = -2.8E-14 (gr1a,2b)==(gr1a,2a)= 0.225806 (gr2a,2b)=.-2.8E-14**	**(gr1a,1b)= 0.638337 (gr1b,2a)= #NUM! (gr1a,2b)=(gr1a,2a)=0.638337 (gr2a,2b)= #NUM!.**	**0.104478**	**0.95712 (p>0.05)**
ABG 2h PO2 Mean ±SD Range	**75.60±4.748 70-80**	**77.60±4.067 70-81**	**77.80±1.897 76-80**	**79.60±2.131 77-83**	**(gr1a,1b)= 7.948428 (gr1b,2a)= 1.723077 (gr2a,2b)= 25.97206 (gr1a,2b)= 36.15452 (gr1a,2a)= 5.660366**	**(gr1a,1b)= 0.008739 (gr1b,2a)= 0.199956 (gr2a,2b)= 2.13E-05 (gr1a,2b)= 1.77E-06 (gr1a,2a)= 0.024407**	**14.29754**	**4.95E-07 (p<0.01)**

ABG 2h PCO2 Mean ±SD Range	**38.86±2.210 36-42**	**34.20±3.167 30-39**	**32.80±3.028 30-38**	**33.00±2.777 30-38**	**(gr1a,1b)= 21.84291 (gr1b,2a)= 1.53125 (gr2a,2b)= 0.035533 (gr1a,2b)= 40.88604 (gr1a,2a)= 39.19155**	**(gr1a,1b)= 6.77E-05 (gr1b,2a)= 0.226202 (gr2a,2b)= 0.851843 (gr1a,2b)= 6.38E-07 (gr1a,2a)= 9.11E-07**	**15.12956**	**2.5E-07 (p<0.01)**
ABG 2h PH Mean ±SD Range	**7.36±.048 7**	**7.30±.000 7**	**7.32±.041 7**	**7.32±.041 7**	**(gr1a,1b)=20.47761 (gr1b,2a)= 3.5 (gr2a,2b)= -2.8E-14 (gr1a,2b)=4.846153846 (gr1a,2a)=20.47761**	**(gr1a,1b)=0.000101 (gr1b,2a)= 0.071854 (gr2a,2b)= #NUM! (gr1a,2b)=0.036116095 (gr1a,2a)=0.000101**	**5.700599**	**0.001772 (p<0.01)**
ABG 4h PO2 Mean ±SD Range	**69.40±6.266 60-79**	**75.40±4.469 67-79**	**75.80±2.883 71-79**	**78.20±1.521 76-80**	**(gr1a,1b)=3 9.117221 (gr1b,2a)= 0.084848 (gr2a,2b)= 8.129032 (gr1a,2b)= 27.94227 (gr1a,2a)= 12.91532**	**(gr1a,1b)= 0.005353 (gr1b,2a)= 0.772978 (gr2a,2b)= 0.00809 (gr1a,2b)= 1.27E-05 (gr1a,2a)= 0.001234**	**12.03599182**	**3.45593E-06 (p<0.01)**
ABG 4h PCO2 Mean ±SD Range	**41.62±2.166 40-45**	**37.40±2.667 35-42**	**34.40±2.414 31-38**	**33.80±2.305 32-38**	**(gr1a,1b)= 22.62903 (gr1b,2a)= 10.43046 (gr2a,2b)= 0.484615 (gr1a,2b)= 91.68669 (gr1a,2a)= 74.33564**	**(gr1a,1b)= 5.39E-05 (gr1b,2a)= 0.003159 (gr2a,2b)= 0.492078 (gr1a,2b)= 2.49E-10 (gr1a,2a)=2.28E-09**	**33.4262289**	**1.62044E-12 (p<0.01)**

ABG 4h PH Mean ±SD Range	**7.32±0.041404 7.3-7.4**	**7.3±1.84E-15 7.3-7.3**	**7.30±0.02582 7.3-7.4**	**7.30±0.035187 7.3-7.4**	**(gr1a,1b)=9.8 3.5 (gr1b,2a)=1 (gr2a,2b)= 0.35 (gr1a,2b)=0.225806 (gr1a,2a)=1.12**	**(gr1a,1b)= 0.071854 (gr1b,2a)= 0.325875 (gr2a,2b)= 0.55886 (gr1a,2b)= 0.638337 (gr1a,2a)=0.298964**	**1.283333**	**0.289017 (p>0.05)**
ABG 8h PO2 Mean ±SD Range	**72.20±1.656 70-75**	**78.60±1.920 75-80**	**77.80±2.957 73-82**	**81.00±1.852 79-84**	**(gr1a,1b)= 95.57333 (gr1b,2a)= 0.772414 (gr2a,2b)= 12.61972 (gr1a,2b)= 188.2222 (gr1a,2a)= 40.95522**	**(gr1a,1b)= 1.58E-10 (gr1b,2a)= 0.386952 (gr2a,2b)= 0.001375 (gr1a,2b)= 5.94E-14 (gr1a,2a)= 6.29E-07**	**44.7311828**	**6.93307E-15 (p<0.01)**
ABG 8h PCO2 Mean ±SD Range	**41.08±1.444 39-43.4**	**30.80±1.207 30-33**	**31.00±2.070 30-35**	**35.20±2.305 33-39**	**(gr1a,1b)= 447.5731 (gr1b,2a)= 0.104478 (gr2a,2b)= 27.5625 (gr1a,2b)= 70.09407 (gr1a,2a)=239.2508**	**(gr1a,1b)= 9.25E-19 (gr1b,2a)= 0.748923 (gr2a,2b)= 1.4E-05 (gr1a,2b)= 4.16E-09 (gr1a,2a)= 3.02E-15**	**106.1122**	**4.42E-23 (p<0.01)**
ABG 8h PH Mean ±SD Range	**7.32± 0.041404 7.3-7.4**	**7.3± 1.84E-15 7.3-7.3**	**7.30± 0.02582 7.3-7.4**	**7.30± 0.035187 7.3-7.4**	**(gr1a,1b)=9.8 3.5 (gr1b,2a)=1 (gr2a,2b)= 0.35 (gr1a,2b)=0.225806 (gr1a,2a)=1.12**	**(gr1a,1b)= 0.071854 (gr1b,2a)= 0.325875 (gr2a,2b)= 0.55886 (gr1a,2b)= 0.638337 (gr1a,2a)=0.298964**	**1.283333**	**0.289017 (p>0.05)**

ABG 12h PO2 Mean ±SD Range	**68.20±3.098 65-73**	**75.40±2.131 72-78**	**74.80±3.610 70-80**	**78.20±1.373 76-80**	**(gr1a,1b)= 54.98182 (gr1b,2a)= 0.307317 (gr2a,1b)= . 130.597 (gr2a,1b)= 11.62644 (gr1a,2a)= 28.875**	**(gr1a,1b)= 4.48E-08 (gr1b,2a)= 0.583732 (gr2a,1b)= 4.67E-12 (gr2a,2b)= 0.001992 (gr1a,2a)= 1E-05**	**37.0236**	**2.54E-13 (p<0.01)**
ABG 12h PCO2 Mean ±SD Range	**43.50±1.793 41-46**	**38.20±2.007 35-40**	**34.00±1.464 32-36**	**33.00±1.464 31-35**	**(gr1a,1b)= 58.17455621 (gr1b,2a)= 42.875 (gr2a,2b)= 3.5 (gr1a,2b)= 308.7 (gr1a,2a)= 252.7**	**(gr1a,1b)= 2.62E-08 (gr1b,2a)= 4.25E-07 (gr2a,2b)= 0.071854 (gr1a,2b)= 1.18E-16 (gr1a,2a)= 1.52E-15**	**118.9523**	**2.87E-24 (p<0.01)**
ABG 12h PH Mean ±SD Range	**7.32± 0.041404 7.3-7.4**	**7.3± 1.84E-15 7.3-7.3**	**7.30± 0.02582 7.3-7.4**	**7.30± 0.035187 7.3-7.4**	**(gr1a,1b)=9.8 3.5 (gr1b,2a)=1 (gr2a,2b)= 0.35 (gr1a,2b)=0.225806 (gr1a,2a)=1.12**	**(gr1a,1b)= 0.071854 (gr1b,2a)= 0.325875 (gr2a,2b)= 0.55886 (gr1a,2b)= 0.638337 (gr1a,2a)=0.298964**	**1.283333**	**0.289017 (p>0.05)**
ABG 24h PO2 Mean ±SD Range	**71.80±4.004 68-79**	**79.24±.768 78-80**	**78.80±2.569 76-83**	**81.00±1.852 79-84**	**(gr1a,1b)= 49.96328 (gr2b,2a)= 0.40391 (gr2a,1b)= 7.239316 (gr1a,2b)= 65.2511 (gr1a,2a)= 32.48106**	**(gr1a,1b)= 1.09E-07 (gr2b,2a)= 0.530237 (gr2a,1b)= 0.011891 (gr1a,2b)= 8.53E-09 (gr1a,2a)= 4.12E-06**	**36.98838**	**2.59E-13 (p<0.01)**

ABG 24h PCO2 Mean ±SD Range	**39.40±1.404 37-41**	**35.40±2.667 31-38**	**30.40±.828 30-32**	**30.00±.000 30-30**	**(gr1a,1b)= 26.41509 (gr1b,2a)= 48.07692 (gr2a,2b)= 3.5 (gr1a,2b)= 672.3043 (gr1a,2a)= 190.7904**	**(gr1a,1b)= 1.89E-05 (gr1b,2a)= 1.54E-07 (gr2a,2b)= 0.071854 (gr1a,2b)= 4.06E-21 (gr1a,2a)= 5.03E-14**	**122.6433**	**1.37E-24 (p<0.01)**
ABG 24h PH Mean ±SD Range	**7.32± 0.041404 7.3-7.4**	**7.3± 1.84E-15 7.3-7.3**	**7.30± 0.02582 7.3-7.4**	**7.30± 0.035187 7.3-7.4**	**(gr1a,1b)=9.8 3.5 (gr1b,2a)=1 (gr2a,2b)= 0.35 (gr1a,2b)=0.225806 (gr1a,2a)=1.12**	**(gr1a,1b)= 0.071854 (gr1b,2a)= 0.325875 (gr2a,2b)= 0.55886 (gr1a,2b)= 0.638337 (gr1a,2a)=0.298964**	**1.283333**	**0.289017 (p>0.05)**

Data are presented as number; shown as mean± SD, numbers and ranges.

This table shows that ABG (PO2, PCO2, PH) preoperative of all patients showed non statistically significant difference between groups (p>0.05) while a high statistically significant difference between ABG (PACU admission, 2h, 4h, 8h, 12h and at 24h). After comparisons between four groups group 2b was the group of high significance between four groups which showed the highest ABG values while group1a the group of low significance between four groups which showed the lowest ABG values.

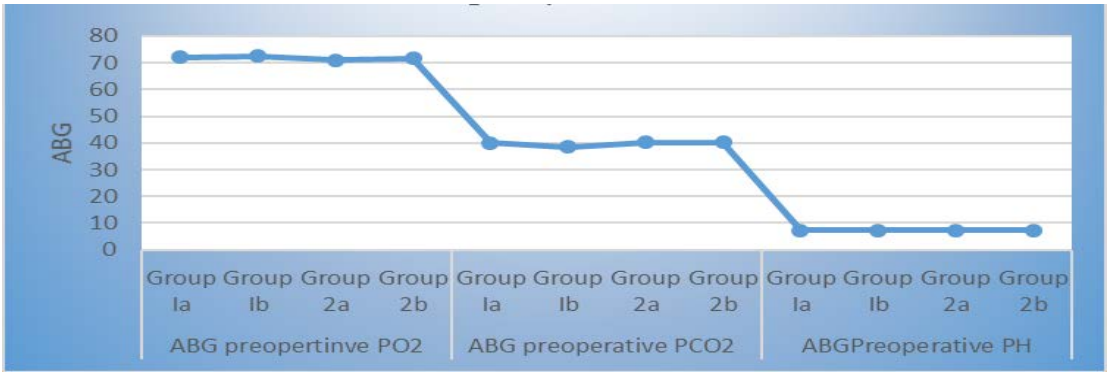


Fig. (42) Mean of ABG preoperative of studied groups

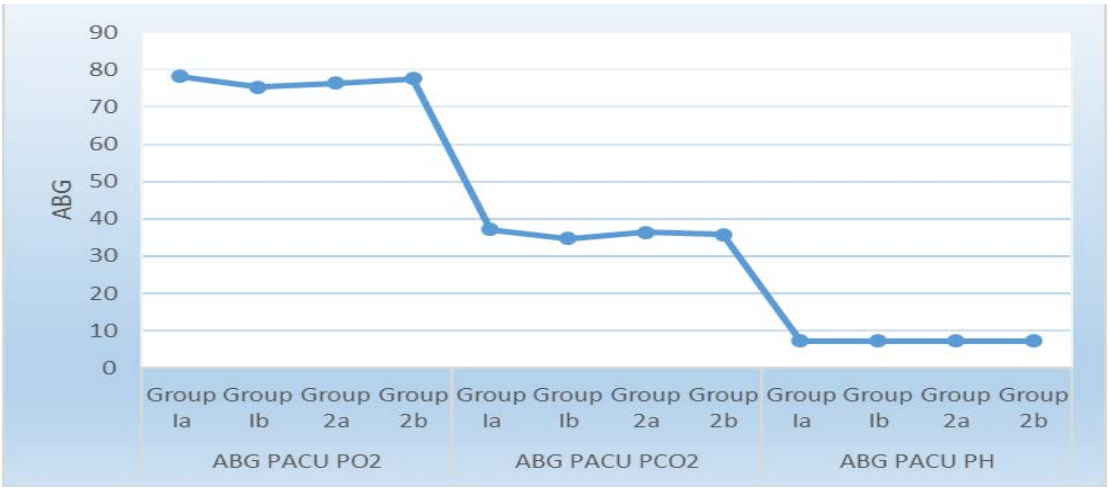


Fig. (43) Mean of ABG PACU of studied groups

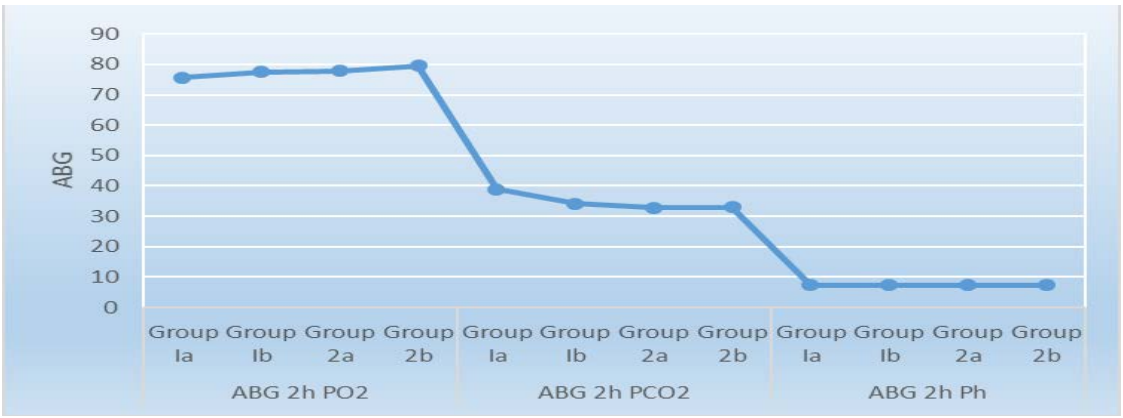


Fig. (44) Mean of ABG 2h of studied groups

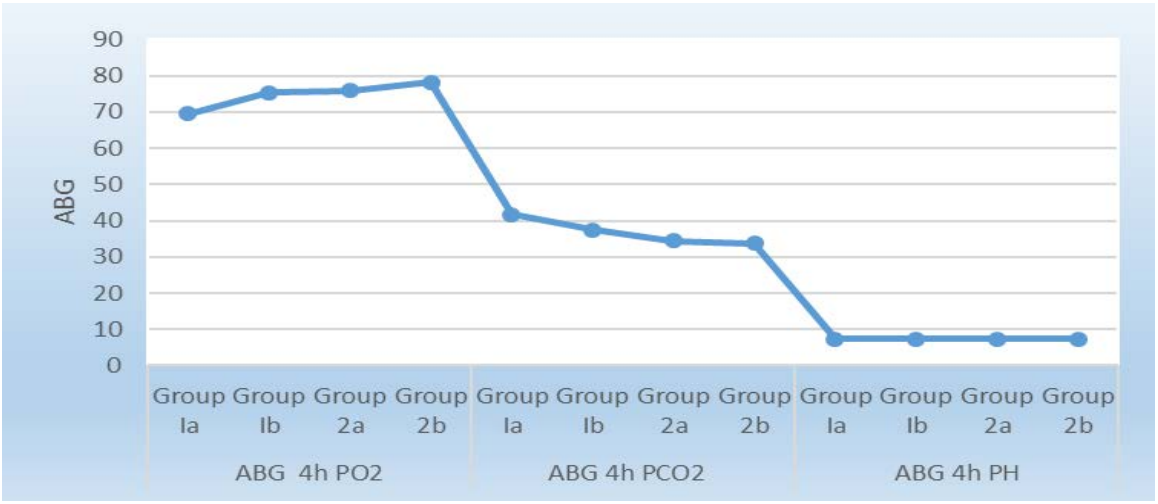


Fig. (45) Mean of ABG 4h of studied groups

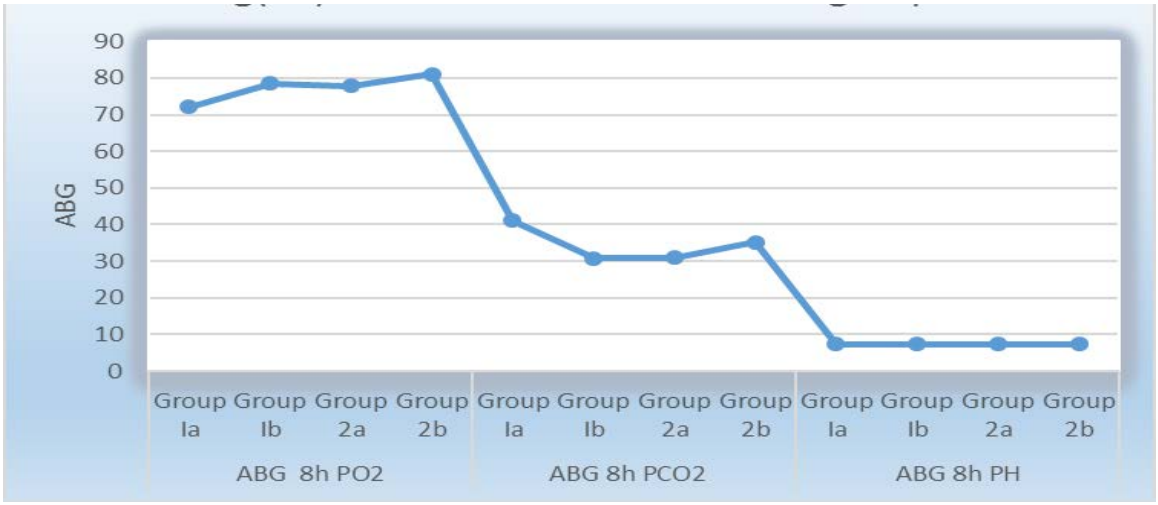


Fig. (46) Mean of ABG 8h of studied groups

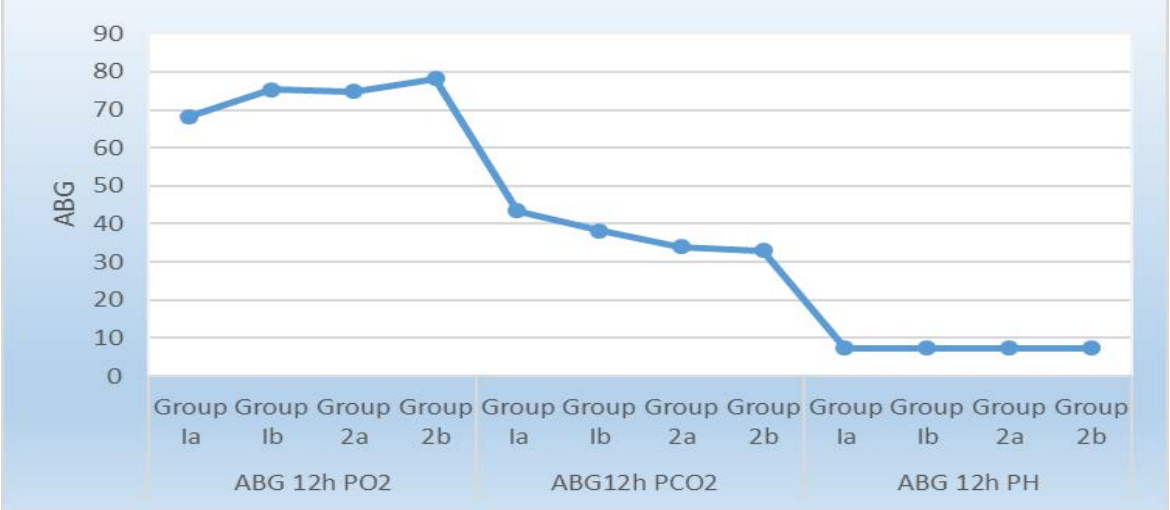


Fig. (47) Mean of ABG 12h of studied group

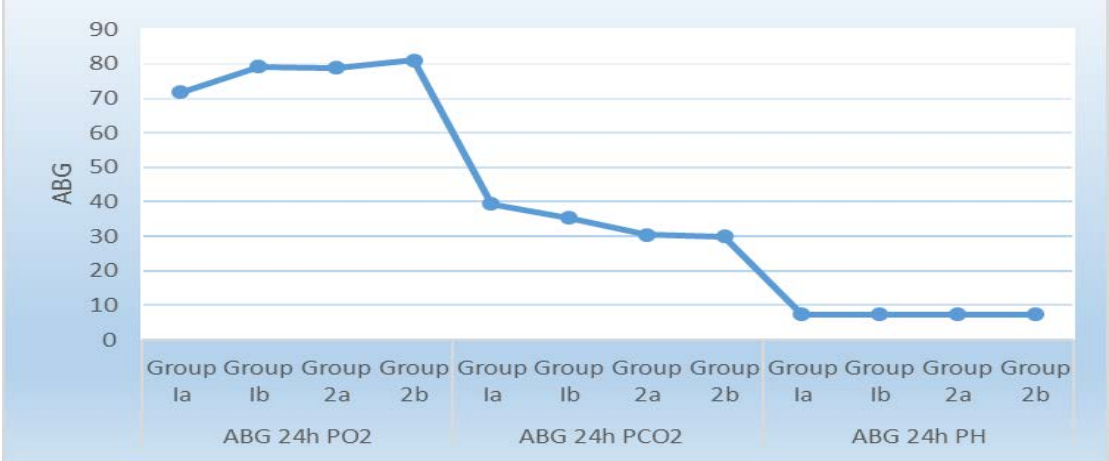


Fig. (48) Mean of ABG 24h of studied groups

Respiratory functions (RF) :

Also the RF was compared at preoperative, PACU admission, 2h, 4h, 8h, 12h and at 24h as shown in table (13).

Table (13) Respiratory function (RF) of the studied groups

Variables	Group Ia N=15	Group Ib N=15	Group 2a N=15	Group 2b N=15	F test (between groups)	Significance	F test	P-value
RF preoperative FEV1 Mean ±SD Range	2.718667 ± 0.156153 2.4 - 2.9	2.670667 ± 0.193777 2.3 - 2.93	2.655333 ± 0.144166 2.4 - 2.9	2.708 ± 0.156351 2.4 - 2.91	(gr1a,1b)= 0.558019 (gr1b,2a)= 0.060457 (gr1a,2b)= 0.034952 (gr2a,2b)=0.919901 (gr1a,2a)= 1.332075	(gr1a,1b)= 0.461287 (gr1b,2a)= 0.807568 (gr1a,2b)= 0.853045 (gr2a,2b)=0.34571 (gr1a,2a)= 0.258193	0.505378 Fvrit= 2.769430949	0.680148 (P>0.05)
RF preoperative PEFR Mean ±SD Range	3.976 ± 0.231911 3.54 - 4.3	4 ± 0.282843 3.5 - 4.5	3.913333 ± 0.247463 3.5 - 4.3	4.06 ± 0.250143 3.7 - 4.5	(gr1a,1b)= 0.064582 (gr1b,2a)= 0.797707 (gr2a,2b)= 2.606154 (gr1a,2b)= 0.909635596 (gr1a,2a)= 0.512139	(gr1a,1b)= 0.801252 (gr1b,2a)= 0.379392 (gr2a,2b)= 0.117664 (gr1a,2b)= 0.348372947 (gr1a,2a)= 0.48014	0.857582	0.468533 (P>0.05)
RF preoperative FVC Mean ±SD Range	3.31 ± 0.118201 3.11 - 3.52	3.386 ± 0.141714 3.18 - 3.63	3.328 ± 0.10297 3.12 - 3.46	3.386667 ±. 0.128434 3.11 - 3.67	(gr1a,1b)= 1.644413 (gr1b,2a)= 1.644413 (gr2a,2b)= 1.905177 (gr1a,2b)= 2.893873 (gr1a,2a)= 0.197768	(gr1a,1b)= 0.210236 (gr1b,2a)= 0.210236 (gr2a,2b)= 0.178421 (gr1a,2b)= 0.099999 (gr1a,2a)= 0.659947	1.535836	0.215277 (P>0.05)
RF PACU FEV1 Mean ±SD Range	1.27 ±.458 p=..008 1 - 2	1.27 ±.458 p=..008 1 - 2	1.40±.507 1 - 2	1.27±.458 1 - 2	(gr1a,2b)=1.91 (gr2a,2b)=.459 (gr1a,2b)=1.91 (gr1a,1b)=9.94 (gr1a,2a)= 0.571429	(gr1a,2b)=.510 (gr2a,2b)=.510 (gr1a,2b)=.183 (gr1a,1b)= .008 (gr1a,2a)=0.456005	0.301075269 F crit=2.769430949	0.824475 p>0.05
RF PACU PEFR Mean ±SD Range	2.718667 ± 0.156153 2.4 - 2.9	2.670667 ± 0.193777 2.3 - 2.93	2.655333 ± 0.144166 2.4 - 2.9	2.708 ± 0.156351 2.4 - 2.91	(gr1a,1b)= 0.558019 (gr1b,2a)= 0.060457 (gr1a,2b)= 0.034952 (gr2a,2b)=0.919901 (gr1a,2a)= 1.332075	(gr1a,1b)= 0.461287 (gr1b,2a)= 0.807568 (gr1a,2b)= 0.853045 (gr2a,2b)=0.34571 (gr1a,2a)= 0.258193	0.505378 Fvrit= 2.769430949	0.680148 (P>0.05)

RF PACU FVC Mean ±SD Range	**1.88±.421 1-3**	**1.84±.267 2-2**	**1.86±.140 2-2**	**1.88±.138 2-2**	**(gr1a,1b)= 116.155 (gr1b,2a)= 12.25383 (gr2a,2b)= 58.89305 (gr1a,2b)= 297.5877 (gr1a,2a)= 198.5715**	**(gr1a,1b)= 1.8E-11 (gr1b,2a)= 0.001574 (gr2a,2b)= 2.33E-08 (gr1a,2b)= 1.89E-16 (gr1a,2a)= 3.08E-14**	**0.076571201**	0.**972389227 (P>0.05)**
RF 2h PEFR Mean ±SD Range	**2.44±.108 2-3**	**2.06±.253 2-3**	**2.18±.457 2-3**	**2.37±.744 2-4**	**(gr1a,1b)= 4.69141 (gr1b,2a)= 1.847328 (gr2a,2b)= 16.41943 (gr1a,2b)= 22.69956 (gr1a,2a)= 7.589242**	**(gr1a,1b)= 0.038982 (gr1b,2a)= 0.184942 (gr2a,2b)= 0.000365 (gr1a,2b)= 5.28E-05 (gr1a,2a)= 0.010203**	13.33801	1.11E-06 (P<0.01)
RF 2h FVC Mean ±SD Range	1.248 ± 0.029568 **1.2-1.29**	**1.323333 ± 0.024689 1.28 - 1.36**	**1.346667 ± 0.031091 1.29 - 1.4**	**1.456 ± 0.036801 1.4 - 1.53**	**(gr1a,1b)= 57.37035 (gr1b,2a)= 5.181269 (gr2a,2b)= 77.25564 (gr1a,2b)= 291.2 (gr1a,2a)=79.32126**	**(gr1a,1b)= 2.99E-08 (gr1b,2a)= . 0.030677 (gr2a,2b)= 1.53E-09 (gr1a,2b)= 2.49E-16 (gr1a,2a)=1.16E-09**	116.6602	4.59E-24 **(P<0.01)**
RF4h FEV1 Mean ±SD Range	**1.76±.407 1-2**	**1.72±.349 1-2**	**1.52±.201 1-2**	**1.64±.143 2-2**	**(gr1a,1b)= 62.56406 (gr1b,2a)= 0.355263 (gr2a,2b)= 113.893 (gr1a,2b)= 117.6824 (gr1a.2a)=65.8796**	**(gr1a,1b)= 1.29E-08 (gr1b,2a)= 0.555937 (gr2a,2b)= 2.25E-11 (gr1a,2b)= 1.55E-11 (gr1a.2a)=7.76E-09**	81.43142	2.07E-20 **(P<0.01)**
RF4h PEFR Mean ±SD Range	**2.26±** 0.076139 **2.11-2.35**	**2.339333 ± 0.027894 2.29-2.39**	**2.375333 ± 0.028752 2.31-2.42**	**2.445333 ± 0.043731 2.38 - 2.51**	**(gr1a,1b)= 12.26825 (gr1b,2a)= 12.11395 (gr1a,2b)= 62.57282 (gr2a,2b)= 26.83414 (gr1a,2a)= 27.07002**	**(gr1a,1b)= 0.001566 (gr1b,2a)= 0.001658 (gr1a,2b)= 1.29E-08 (gr2a,2b)= 1.69E-05 (gr1a,2a)= 1.59E-05**	35.92546	4.42E-13 **(P<0.01)**
RF4h FVC Mean ±SD Range	**1.29±** 0.027377 **1.16-1.24**	**1.3± 0.026726 1.25-1.34**	**1.32± 0.026726 1.27-1.34**	**1.41±. 0.028536 1.35-1.45**	**(gr1a,1b)= 101.1106 (gr1b,2a)= 4.2 (gr2a,2b)= 79.48598 (gr1a,2b)= 420.324 (gr1a,2a)= 145.9252**	**(gr1a,1b)= 8.52E-11 (gr1b,2a)= 0.049897 (gr2a,2b)= 1.14E-09 (gr1a,2b)= 2.12E-18 (gr1a,2a)= 1.27E-12**	147.9223	1.38E-26 **(P<0.01)**
RF8h FEV1 Mean ±SD Range	**1.88±.421 1-3**	**1.84±.267 2-2**	**1.86±.140 2-2**	**1.88±.138 2-2**	**(gr1a,1b)= 116.155 (gr1b,2a)= 12.25383 (gr2a,2b)= 58.89305 (gr1a,2b)= 297.5877 (gr1a,2a)= 198.5715**	**(gr1a,1b)= 1.8E-11 (gr1b,2a)= 0.001574 (gr2a,2b)= 2.33E-08 (gr1a,2b)= 1.89E-16 (gr1a,2a)= 3.08E-14**	**0.076571201**	0.**972389227 (P>0.05**)

RF8h PEFR Mean ±SD Range	**2.42±.211 2-3**	**2.36±.311 2-3**	**2.62±.446 2-3**	**89.00±179.071 2-435**	**(gr1a,1b)= 33.22985 (gr1b,2a)= 1.520566 (gr2a,2b)= 23.60506 (gr1a,2b)=. 101.9062 (gr1a,2a)= 49.12095**	**(gr1a,1b)= 3.45E-06 (gr1b,2a)= 0.227787 (gr2a,2b)=. . 4.08E-05 (gr1a,2b)=. 7.81E-11 (gr1a,2a)= 1.27E-07**	**3.503056**	**0.021146 (P<0.05)**
RF8h FVC Mean ±SD Range	**1.386± 0.036214 1.33-1.44**	**1.506 ±0.039785 1.44-1.56**	**1.573333 ± 0.03658 1.5-1.78**	**1.72± 0.024842 1.7-1.78**	**(gr1a,1b)= 74.62981 (gr1b,2a)= 23.28236 (gr2a,2b)= 218.2479 (gr1a,2b)= 985.7244 (gr1a,2a)= 198.6797**	**(gr1a,1b)= 2.19E-09 (gr1b,2a)= 4.47E-05 (gr2a,2b)= 9.55E-15 (gr1a,2b)= 2.28E-23 (gr1a,2a)= 3.06E-14**	**273.1278**	2.17E-33 **(P<0.01)**
RF12h FEV1 Mean ±SD Range	**1.80±.596 1-3**	**1.58±.231 1-2**	**1.60±..196 1-2**	**1.74±.182 2-2**	**(gr1a,1b)= 66.05643 (gr1b,2a)= 5.136084 (gr2a,2b)= 232.9283175 (gr1a,2b)= 330.0533193 (gr1a,2a)= 94.46862**	**(gr1a,1b)= 7.55E-09 (gr1b,2a)= 0.031988 (gr2a,2b)= 4.23E-15 (gr1a,2b)= 4.96467E-17 (gr1a,2a)= 1.8E-10**	**175.0369**	2.04E-28 **(P<0.01)**
RF12h PEFR Mean ±SD Range	**2.16±..124 2-2**	**2.08±..137 2-2**	**2.40±..398 2-3**	**2.66±..924 2-4**	**(gr1a,1b)= 35.38431 (gr1b,2a)= 33.01859 (gr2a,2b)= 36.90732878 (gr1a,2b)= 426.3971 (gr1a,2a)= 128.093**	**(gr1a,1b)= 2.1E-06 (gr1b,2a)= 3.63E-06 (gr2a,2b)= 1.49546E-06 (gr1a,2b)= 1.75E-18 (gr1a,2a)= 5.85E-12**	3.947328023	0.012646 (P<0.01)
RF12h FVC Mean ±SD Range	**1.11±..046 1-1**	**1.52±..310 1-2**	**1.38±.199. 1-2**	**1.48±.181. 1-2**	**(gr1a,1b)= 76.83864 (gr1b,2a)= 62.658 (gr2a,2b)= 50.03719 (gr1a,2b)= 565.2405 (gr1a,2a)= 281.8422**	**(gr1a,1b)= 1.62E-09 (gr1b,2a)= . 1.27E-08 (gr2a,2b)= 1.07E-07 (gr1a,2b)= 4.16E-20 (gr1a,2a)= 3.78E-16**	**11.95837727**	**3.70305E-06 (P<0.01)**
RF24h FEV1 Mean ±SD Range	**2.18±..513 2-3**	**2.00±..217 2-2**	**2.14±..192 2-3**	**2.13±..233 2-3**	**(gr1a,1b)= 33.73941 (gr1b,2a)= 1.388679 (gr2a,2b)= 11.07835 (gr1a,2b)= 69.48452 (gr1a,2a)= 32.43254**	**(gr1a,1b)= 3.07E-06 (gr1b,2a)= 0.248546 (gr2a,2b)= 0.002455 (gr1a,2b)= 4.54E-09 (gr1a,2a)= 4.17E-06**	**38.49694**	**1.23E-13 (P<0.01)**

RF24h PEFR Mean ±SD Range	**2.74±..124 3-3**	**2.46±..140 2-3**	**2.86±..350 3-3**	**3.03±..787 2-4**	**(gr1a,1b)= 67.49151 (gr1b,2a)= 1.444422 (gr2a,2b)= 59.53982 (gr1a,2b)= 208.4346 (gr1a,2a)= 70.74389**	**(gr1a,1b)= 6.09E-09 (gr1b,2a)= 0.239492 (gr2a,2b)= 2.09E-08 (gr1a,2b)= 1.69E-14 (gr1a,2a)= 3.79E-09**	**4.419833**	**0.007369 (P<0.01)**
RF 24h FVC Mean ±SD Range	**1.40±.185 1-2**	**1.88±.288 2-2**	**1.80±.160 2-2**	**1.90±.130 2-2**	**(gr1a,1b)= 73.65564 (gr1b,2a)= 44.46141 (gr2a,2b)= 81.39979118 (gr1a,2b)= 249.7541 (gr1a,2a)= 158.8731**	**(gr1a,1b)= 2.50882E-09 (gr1b,2a)= 3.09E-07 (gr2a,2b)= 8.86765E-10 (gr1a,2b)= 1.76E-15 (gr1a,2a)= 4.63E-13**	**20.62053013**	**3.97444E-09 (P<0.01)**

Data are presented as number; shown as mean± SD, numbers and ranges.

This table shows that RF (FEV1, PEFR, FVC) preoperative, at PACU admission, RF 8h FEV1, RF 12h FEV1, RF 24h FEV1 of all patients showed non-significant difference ($p>0.05$) within or between groups while a highly statistically significant ($P<0.01$) difference between groups regarding RF 2h, 4h, RF 8h PEFR, RF 8h FVC, RF 12h PEFR, RF 12h FVC, RF 24h PEFR, RF 24h FVC. After comparisons between four groups group 2b was the group of high significance which showed the highest respiratory function values between four groups while group1a the group of low significance which between four groups which showed the least values of respiratory functions.

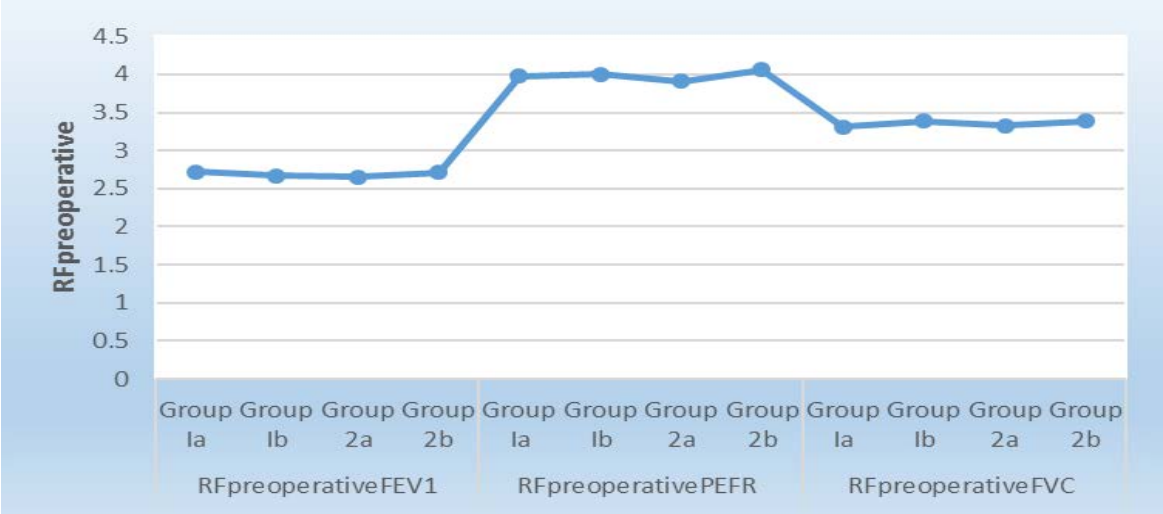


Fig. (49) Mean of RF preoperative of studied groups

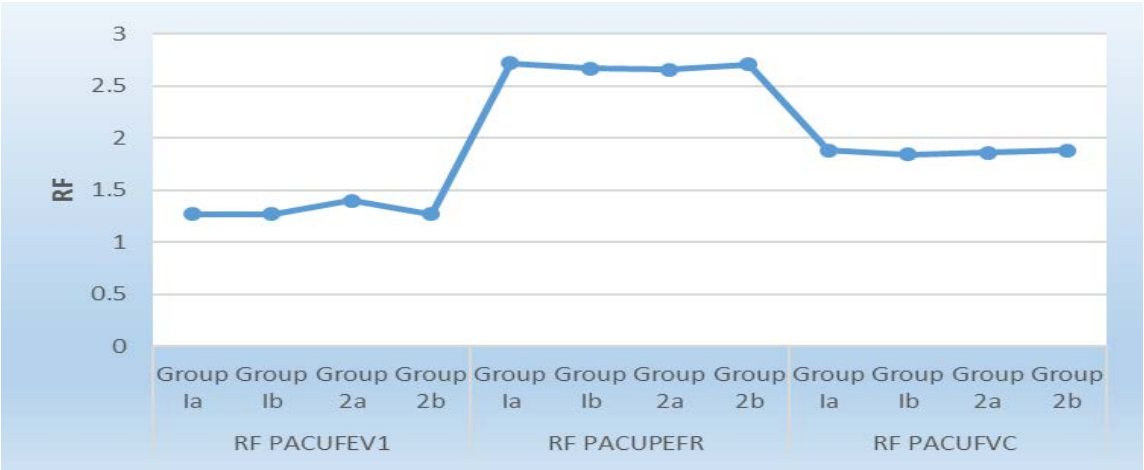


Fig. (50) Mean of RF PACU of studied groups

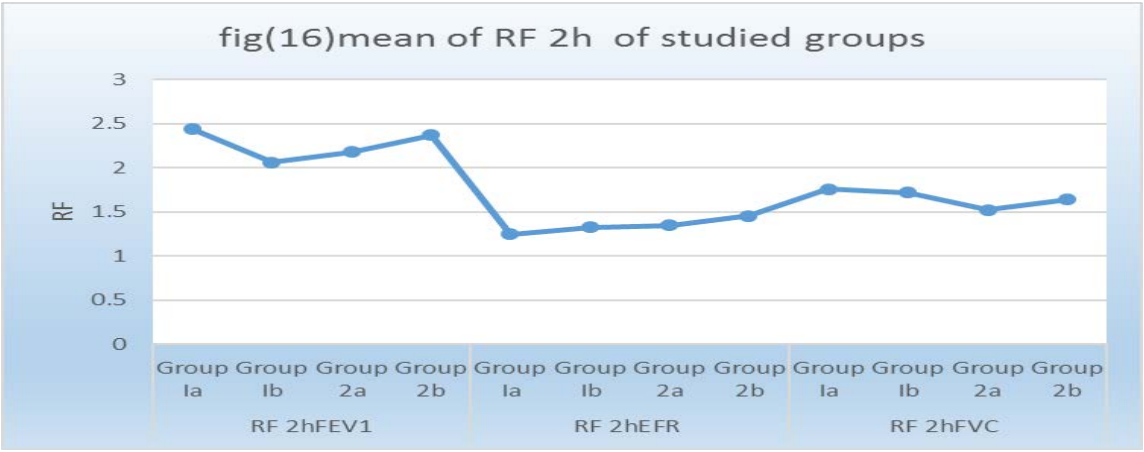


Fig. (51) Mean of RF 2h of studied groups

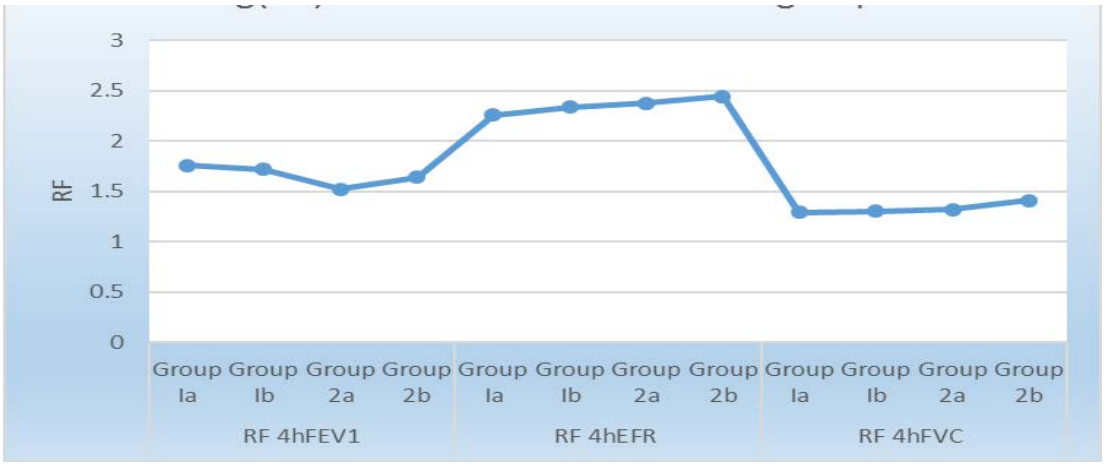


Fig. (52) Mean of RF 4h of studied groups

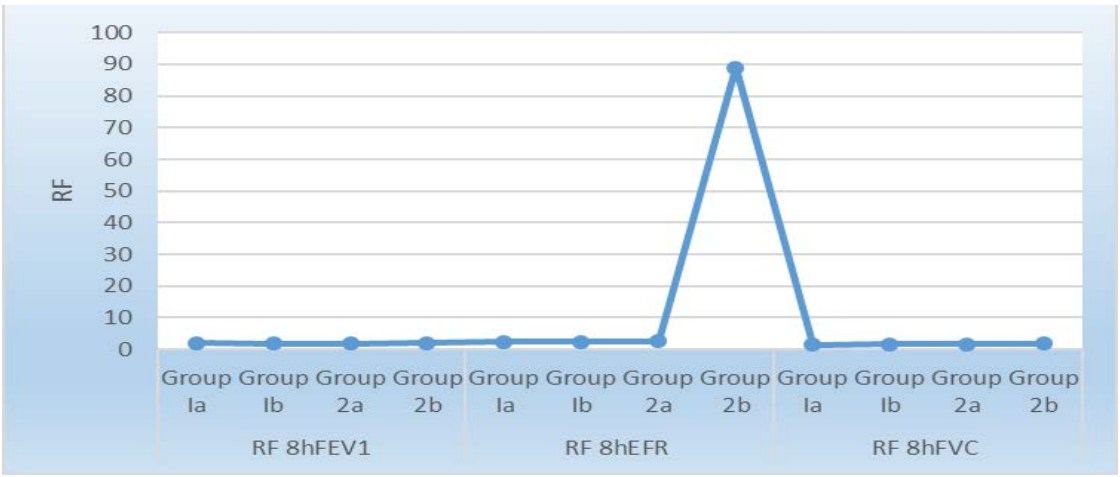


Fig. (53) Mean of RF 8h of studied groups

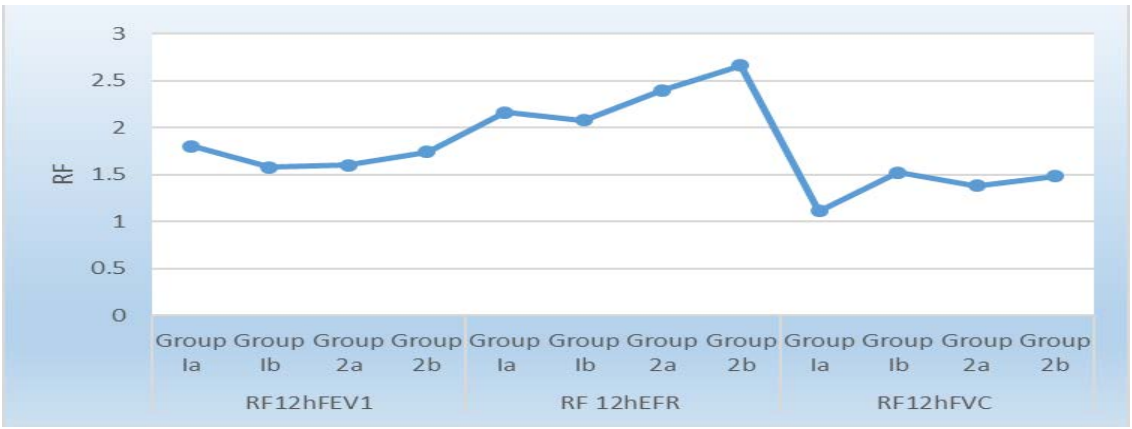


Fig. (54) Mean of RF of 12h of studied groups

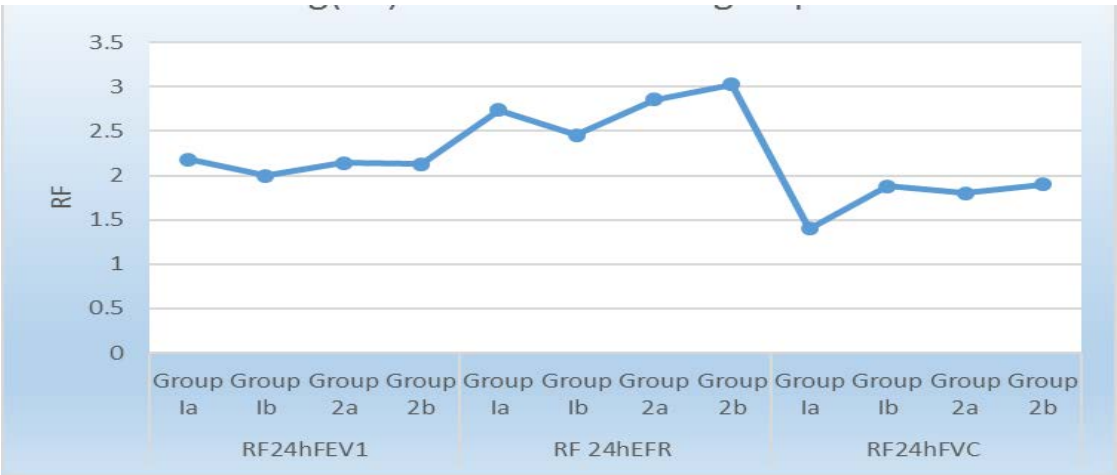


Fig. (55) Mean of RF of studied groups

Blood cortisol level:

Also blood cortisol level was compared at preoperative, 10 min after the block and 4h after extubation as shown in table (14).

Table (14): Blood cortisol level (ug/dl) among the studied groups.

Variables	Group Ia N=15	Group Ib N=15	Group 2a N=15	Group 2b N=15	F test (between groups)	SIG	F test	P-value
Blood cortisol level preoperative Mean ±SD Range	13.06± 0.408248 12.5-13.9	13.09± 0.436654 12.5-13.9	13.2± 0.360555 12.7-13.9	13.2± 0.399046 12.6-13.9	(gr1a,1b)= 0.029851 (gr1a,2a)= 0.898876 (gr1a,2b)= 0.902104 (gr2a,2b)= 0.002305 (gr2a,1b)= 0.532225	(gr1a,1b) =0.864072 (gr1a,2a) =0.351195 (gr1a,2b) =0.350345 (gr2a,2b) =0.96205 (gr2a,1b) =0.471732	0.482202 Fcrit= 2.769431	0.695984 (P>0.05)
Blood cortisol level 10 min after block Mean ±SD Range	12.85333333 ± 0.65232186 11.6-13.9	12.48± 0.781208 11.4-13.6	12.56± 0.629966 11.3-13.4	12.82± 0.603798 11.7-13.9	(gr1a,1b)= 2.018389 (gr1a.2a)= 1.569427 (gr1b,2a)= 0.095319 (gr1a,2b)= 0.021095 (gr2a,2b)= 1.331707	(gr1a,1b) =0.166445 (gr1a.2a) =0.220652 (gr1b,2a) =0.759806 (gr1a,2b) =0.885562 (gr2a,2b) =0.258257	1.157702	0.334049 (p>0.05)
Blood cortisol level 4h after extubation Mean ±SD Range	27.06 ± 0.453242 26.3-27.8	25.68 ± 0.40918 25-26.3	25.71333 ± 0.523541 25-26.7	24.82 ± 0.507374 24-25.8	(gr1a,1b) =76.61379 (gr1a,2a)= 56.7285 (gr2a,1b)= 0.037748 (gr1a,2b)= 162.6074 (gr2a,2b)= 22.52141	(gr1a,1b) =.1.67E09 (gr1a,2a) =3.33E-08 (gr2a,1b) =0.847353 (gr1a,2b) =3.51E-13 (gr2a,2b) = 5.56E05	56.80276 F crit=2.769430949	5.43E-17 P<0.01

Data are presented as number; shown as mean± SD, numbers and range.

This table shows statistically non-significant difference (P>0.05) between the four groups regarding to preoperative Blood cortisol level , Blood cortisol level 10 min after block while Blood cortisol level 4h after extubation was high statistically significant (p<0.01) of all patients showed difference within or between , After comparisons between four groups group 2b was the group of high significance between four groups which showed the lowest blood cortisol level while group1a the group of low significance between four groups which showed the highest blood cortisol level.

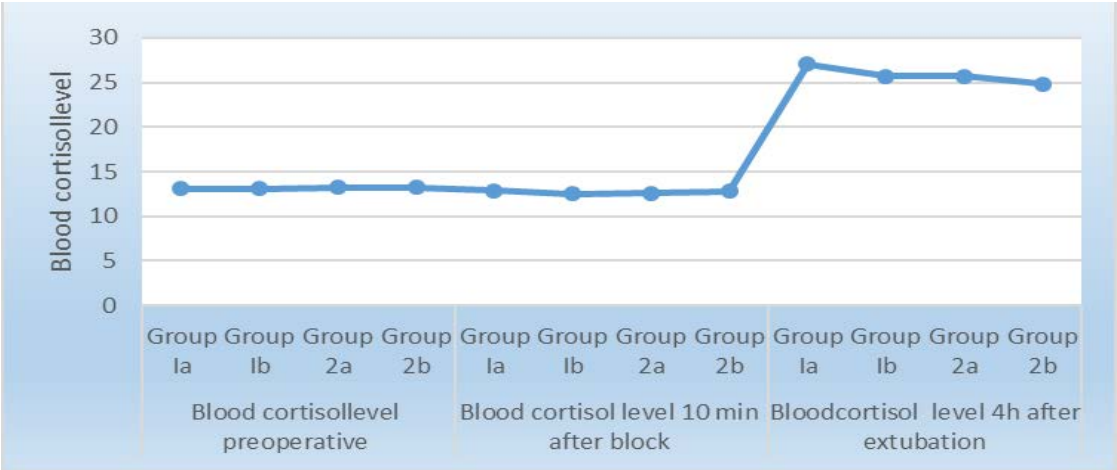


Fig. (56) Mean of Blood cortisol level of studied groups (ug/dl)

Discussion

Pain after thoracotomy is very severe, probably the most severe pain experienced after surgery. It is also unique as this pain state has multiple implications, including respiratory failure due to splinting; inability to clear secretions by effective coughing, with resulting pneumonia; and facilitation of the often incapacitating chronic pain: the post-thoracotomy pain syndrome. A thoracotomy requires a very painful incision, involving multiple muscle layers, rib resection, and continuous motion as the patient breathes **(Peter, 2008).**

Treatment of acute post-thoracotomy pain is particularly important not only to keep the patient comfortable but also to minimize pulmonary complications. Many methods of pain management, each with attendant problems, have been tried with varied success, for example: intercostal nerve block, intrapleural analgesia, cryo-analgesia, lumbar epidural, thoracic epidural, paravertebral block, IV narcotics, intrathecal or epidural narcotics, NSAIDS and transcutaneous nerve stimulation. There are different analgesic modalities for management of post-thoracotomy pain. There are systemic methods which includes infusion and patient-controlled analgesia (PCA) or regional techniques that mainly rely on epidural, intrathecal or paravertebral blocks. Other techniques range from intercostal nerve block to cryoprobeneurolysis.

Our study which was done on 60 patients undergoing thoracotomy operation they were divided into two groups(US guided continuous intercostal nerve block and US guided continuous thoracic paravertebral nerve block)each were subdivided into another two sub groups one received bupivacaine and the other received bupivacaine with dexmedetomidine.

Continuous intercostal nerve block (INB) and Continuous thoracic paravertebral nerve block (TPVB) methods, being one of the components of the analgesia strategy, are quite effective techniques in managing the postthoracotomy pain. There was statistically significant difference in the two methods in terms of efficient analgesia, respiratory functions and stress response to surgeryin favor of TPVB which showed greater analgesic, more improvement of respiratory function, more hemodynamic and respiratory stability than intercostal block especially after adding dexmedetomedine in patients having thoracotomy. We recommend that the TPVB with dexmedetomedine is safe and effective and should be always considered as an intercostal nerve block alternative.

Our results go with **(Moawadand Taha, 2015)** who studied comparison of paravertebral block against intercostal block for postoperative pain relief in open renal surgery.PVB and ICB are safe analgesic techniques, and they decrease the postoperative pain score and analgesic requirements after open renal surgery. PVB provides more patient satisfaction and a longer duration of analgesia postoperatively.

(Hassan and Mahran, 2017) studied evaluation of the role of dexmedetomidine in improvement of the analgesic profile of thoracic paravertebral block in thoracic surgeries. Addition of dexmedetomidine to paravertebral bupivacaine in patients undergoing thoracic surgeries provides more effective analgesia with improvement in post-operative pulmonary functions.

(Ramsay et al., 2014) who studied the effect of paravertebral administration of dexmedetomidine as an adjuvant to local anesthetic on the intraoperative anesthetic drug requirement and incidence of post-thoracotomy pain syndrome. Paravertebral dexmedetomidine

administration resulted in decreased intraoperative anesthetic drug requirement, less pain, and lower requirements of supplemental opioid in the postoperative period. However, it had no effect on the incidence of post-thoracotomy pain syndrome.

(Matthews PJ et al., 1989) who studiedParavertebral thoracic block was found to be an accurate, simple and safe method which carries significant advantages over intercostal or epidural block. Continuous paravertebral infusion was compared with extradural infusion of bupivacaine for post-thorocotomy pain relief and found to have comparable results in terms of analgesia.Paravertebral bupivacaine was demonstrated superior to epidural bupivacaine in terms of analgesia, pulmonary function, neuroendocrine stress response, side-effects and post- operative respiratory morbidity in patients following thoracotomy.

(Karmakar et al., 2003) who studied the efficacy of a continuous thoracic paravertebral infusion of bupivacaine for pain management in patients with unilateral multiple fractured ribs. Results confirmed that continuous thoracic paravertebral infusion of bupivacaine is a simple and effective method of providing continuous pain relief in patients with unilateral multiple fractured ribs. It also produced a sustained improvement in respiratory parameters and oxygenation.

(Pusch F et al.,1999) studied single-injection unilateral PVB given at the level of T4, as a sole anesthetic technique, for patients undergoing breast surgery for breast malignancy. Time for performance of blocks lasted from 4 to 9 min. Recovery from anesthesia or sedation was shortened, while postoperative pain scores (VAS), the incidence of vomiting and the requirement for analgesics were lower in the paravertebral group.

(Ali et al., 2016) who studied pre-emptive analgesia of ultrasound-guided pectoral nerve block II with dexmedetomidine-bupivacaine for controlling chronic pain after modified radical mastectomy. A total of 60 female patients were randomized into two groups: group C (the control group) and group BD (the bupivacaine–dexmedetomidine group). Group BD showed highly significant reduction in intubation heart rate, intubation mean arterial blood pressure, intraoperative heart rate, intraoperative mean arterial blood pressure, and total fentanyl dose (μg).

(Yong et al., 2017)who studied the effect of low dose of dexmedetomidine as an adjuvant to bupivacaine in cesarean surgery provides better intraoperative somato-visceral sensory block characteristics and postoperative analgesia. This study aimed to investigate the beneficial effects of dexmedetomidine on somato-visceral sensory block characteristcs, postoperative analgesia and stress response of intrathecal bupivacaine administration in women undergoing cesarean section, and to find out which dose is better.

(De Cosmo et al., 2012) who studied postoperative analgesia in thoracic surgery: A comparison between continuous paravertebral nerve block and continuous incisional infusion with OnQ Pain Relief System. Continuous incisional infusion of local anesthetic is not as effective as paravertebral analgesia after thoracotomy.

(Dutta et al., 2017) who studied the effect of paravertebral administration of dexmedetomidine as an adjuvant to local anesthetic on the intraoperative anesthetic drug requirement and incidence of post-thoracotomy pain syndrome. Paravertebral dexmedetomidine administration resulted in decreased intraoperative anesthetic drug requirement, less pain, and lower requirements of supplemental opioid in

the postoperative period. However, it had no effect on the incidence of post-thoracotomy pain syndrome.

(Elizabeth et al., 1995) that studied Continuous extrapleural intercostal block (EPIB) with bupivacaine has been reported to be an effective analgesic technique in patients after thoracotomy. Continuous EPIB with lidocaine appears to be a promising adjuvant technique in the management of postthoracotomy pain. Effectiveness needs to be confirmed in a prospective randomized study.

(Mohamed et al., 2014) that studied the efficacy and tolerability of the addition of adjunctive analgesic agents in paravertebral analgesia. The addition of adjunctive analgesics, such as fentanyl and clonidine, to local anesthetics has been shown to enhance the quality and duration of sensory neural blockades, and decrease the dose of local anesthetic and supplemental analgesia.

(Ali Hassan et al., 2016) who studied pre-emptive analgesia of ultrasound-guided pectoral nerve block II with dexmedetomedine-bupivacaine for controlling chronic pain after modified radical mastectomy. Reduced visual analogue scale was seen at the first 24 h postoperatively, with significant reduction in total postoperative analgesiaand delayed rescue analgesia in the bupivacaine dexmedetomidine group (the BD group) in relation to the control group. This marked reduction in the severity of postoperative pain correlates with reduced chronic pain on follow-up of our patients with patient satisfaction, good sleep, and reduced analgesic need, which improves quality of life.

(Sabanathan et al., 1990) who studied efficacy of continuous extrapleural intercostal nerve block on post-thoracotomy pain and

pulmonary mechanics. After thoracotomy, continuous intercostal blockade with bupivacaine is a safe and effective method of pain relief which reduces the early loss of postoperative pulmonary function significantly and more rapidly restores respiratory mechanics.

(Jakobsonet al., 1980) who studied effects of intercostal nerve blocks on pulmonary mechanics in healthy men.It is concluded that the nerve block had no obvious effects on pulmonary mechanics, the changes observed rather being attributable to effects on the chest wall.

(Taman et al., 2016) which studied the effects of dexmedetomedine added to bupivacaine for intercostal nerve block in pediatric open heart surgery. Postoperative pain Face, Legs, Activity, Cry, Consolability (FLACC) scores, hemodynamics, opioid consumption, and hospital length of stay were evaluated in all patients.Heart rate, mean arterial pressure, and FLACC score were significantly lower in the dexmedetomidine group compared with the control group after 4 and 8 h in ICU. Duration of intubation and ICU stay were significantly shorter in the dexmedetomidine group compared with the control group. Ramsay sedation score was lower in the dexmedetomidine group compared with the control group at 4 h in ICU. Bradycardia and hypotension incidence were higher in the dexmedetomidine group compared with that in the control group. Adding dexmedetomidine to bupivacaine for parasternal block in pediatric patients submitted to open heart surgery leads to good pain control, less analgesic consumption, early extubation, and short ICU length of stay.

(Wang et al., 2017) who studied intraoperative multiple intercostal nerve blocks exert anesthetic-sparing effect.Less general anesthetic is required in patients with regional blocks than in those without, as

assessed through commonly used anesthesia monitoring parameters such as blood pressure, heart rate, and bispectral index (BIS). With comparable BIS and blood pressure in the subsequent surgical procedure, the adequacy of anesthesia and the anesthetic component provided by intraoperative INBs and vagal nerve could be monitored adequately. The anesthetic-sparing effect of intraoperative nerve blocks can be realized when the Ce of propofol infusion was reduced to the target BIS level.

(Obayah et al., 2010).**Obayah et al**. showed an increase in the time to first analgesic request following greater palatine nerve blocks cleft palate repair in children when bupivacaine plus dexmedetomidine (1 µg/kg) was compared with bupivacaine alone (22 hr vs. 14.2 hr, $p < 0.001$). In addition, pain scores in the dexmedetomidine group were significantly lower for the first 24 hr. There were no differences in sedation scores or hemodynamic variables between the two groups.

(Galway et al.,1975) who studied the effect of intercostal nerve blockade during operation on lung function and relief of pain following thoracotomy. This form of treatment, although free from serious side effects, had no beneficial effects on lung function and is not recommended for the relief of pain following surgery.

(Anis and Anthony, 2016) who studied Thoracic Paravertebral Block, Multimodal Analgesia, and Monitored Anesthesia Care for Breast Cancer Surgery in Primary Lateral Sclerosis. In patients with PLS, thoracic paravertebral block and multimodal analgesia can provide reliable anesthesia and effective analgesia for breast surgery with avoidance of potential risks associated with general anesthesia, muscle paralysis, and opioid use. The patient tolerated the entire surgery

reporting no discomfort or pain and remained hemodynamically stable, with no significant change in respiratory rate or oxygen saturation.

(Piraccini et al., 2011)who studied analgesia for thoracic surgery.We conclude that paravertebral block is superior to intravenous analgesia in providing pain control and preserving postoperative pulmonary function while it is equal to thoracic epidural analgesia regarding this two issues. Paravertebral block has a better safety profile when compared to intravenous and thoracic epidural analgesia. Its effect on chronic pain incidence still needs further studies.

(Bi et al., 2017)who studied Low dose of dexmedetomidine as an adjuvant to bupivacaine in cesarean surgery provides better intraoperative somato-visceral sensory block characteristics and postoperative analgesia. The use of dexmedetomidine especially at the dose of 3μg as an adjuvant to bupivacaine in cesarean surgery provides better intraoperative somato-visceral sensory block characteristcs and postoperative analgesia, which produced no influence on Apgar scores, side effects and stress response.

(Abd EL-Hamid and Azab, 2016) who studied intraoperative haemodynamic stability and stress response to surgery in patients undergoing thoracotomy: comparison between ultrasound-assisted thoracic paravertebral and epidural block.This study aimed to evaluate intraoperative haemodynamics and stress response to thoracotomy in patients receiving thoracic epidural or thoracic paravertebral block. Thoracic paravertebral block is an effective analgesic technique showing greater haemodynamic stability and less stress response to surgery compared with epidural analgesia in patients undergoing thoracotomy.

Our results did not go with **(Morimoto,2015)** who studied regional anesthesia role in the anesthetic management of thoracic

surgeries.Regional anesthesia provides better pain control than systemic opioid analgesia, controls stress response, and prevents respiratory complications.These factors should improve patient outcomes.The first choice of regional anesthesia for thoracic surgery is epidural analgesia or thoracic paravertebral block (TPVB).In general, analgesic efficiency of epidural analgesia and TPVB is equivalent.However, TPVB has some advantage over epidural analgesia including fewer complications.When these two blocks are contraindicated, application of intercostal nerve block or inter-pleural block can be considered.

(Zhan et al., 2017) who studied effect of intercostal nerve block combined with general anesthesia on the stress response in patients undergoing minimally invasive mitral valve surgery.The results suggest that intercostal nerve block combined with general anesthesia conforms to the concept of rapid rehabilitation surgery and may be suitable for clinical practice.

(Chan et al., 1991) who studied analgesic and pulmonary effects of continuous intercostal nerve block following thoractomy. The technique of continuous intercostal nerve block described in this study is an effective treatment for the control of post-thoracotomy pain.

(Ahmed et al., 2017) who studied Role of intercostal nerve block in reducing postoperative pain following video-assisted thoracoscopy. There was 2 groups one received ICNB and the other group received only GA.There was no significant difference in pain scores and morphine consumption between the two groups after 6 hours. Patients receiving intercostal nerve block have better pain control and less morphine consumption as compared to those patients who did not receive intercostal nerve block in early (6 hours) post-operative period.

(Bigler et al., 1989) who studied effects of thoracic paravertebral block with bupivacaine versus combined thoracic epidural block with bupivacaine and morphine on pain and pulmonary function after cholecystectomy. Pain scores were significantly higher in the paravertebral group, as was the need for systemic morphine (P less than 0.05). Pulmonary function estimated by forced vital capacity, forced expiratory volume and peak expiratory flow rate decreased about 50% postoperatively in both groups. In conclusion, the continuous paravertebral bupivacaine infusion used here was insufficient as the only analgesic after cholecystectomy. In contrast, epidural blockade with combined bupivacaine and low dose morphine produced total pain relief in six of ten patients.

(Berrisford et al., 1990) who studied pulmonary complications after lung resection: the effect of continuous extrapleural intercostal nerve block. To assess the efficacy of continuous extrapleural intercostal nerve block (CEINB) with 0.5% bupivacaine on postoperative pain, pulmonary function and pulmonary complications.Pulmonary function recovered earlier in the bupivacaine group. Pulmonary complications occurred in 1 patient with normal lung function and 12 patients with obstructive airways disease (COAD): FEV1/FVC less than 70%. There were no infusion-related complications. CEINB has been shown to be safe and effective in reducing postoperative pain and pulmonary complications. CEINB minimises the loss of lung function after thoracotomy and restores impaired pulmonary mechanics more rapidly.

(Mohamed et al., 2014) that studied the efficacy and tolerability of the addition of adjunctive analgesic agents in paravertebral analgesia. The addition of adjunctive analgesics, such as fentanyl and clonidine, to local anesthetics has been shown to enhance the quality and duration of

sensory neural blockades, and decrease the dose of local anesthetic and supplemental analgesia. The addition of dexmedetomidine 1 μg/kg to bupivacaine 0.25% in thoracic PVB in patients undergoing modified radical mastectomy improves the quality and the duration of analgesia and also provides an analgesic sparing effect with no serious side effects.

(Jinzhuan et al., 2015).who evaluated the efficacy and safety of administration of an intercostal nerve block (INB) with general anesthesia to elderly patients undergoing a distal gastrectomy. Administration of INB with general anesthesia enhanced analgesia, led to stable hemodynamics, and reduced anesthetic consumption and postoperative stress response.

(Garutti et al., 2006) who studied the use of the thoracic paravertebral block (TPVB) in association with general anesthesia for lung-resection surgery. The aim of the study was to evaluate the hemodynamic effects of a 5-mg/kg lidocaine bolus injected in the thoracic paravertebral space during one-lung ventilation (OLV) in noncardiac patients undergoing thoracic surgery. None of the other hemodynamic parameters studied was significantly altered. In non-cardiac patients, TPVB is associated with good hemodynamic stability, despite a small and transient decrease in myocardial contractility that could be related to the drug's systemic effects after its absorption.

(Kulkarni, 2016)who studied regional technique like thoracic paravertebral block for breast surgery is gaining a lot of popularity. As it produces unilateral action thereby minimal hemodynamic changes with autonomic blockade, allows early ambulation, facilitates postoperative analgesia, eliminate the risks/complications of general anesthesia and thus reduces the hospital stay and cost.Single needle continuous thoracic

paravertebral block using ropivacaine 0.5% with dexmeditomidine 0.5 mcg/kg as a sole anesthetic technique provided satisfactory surgical anesthesia with minimal hemodynamic changes and adverse effects in 25 cases of radical mastectomies.

(Sahar et al., 2014) who studied dexmedetomidine as an adjunctive analgesic with bupivacaine in paravertebral analgesia for breast cancer surgery. The addition of dexmedetomidine 1 µg/kg to bupivacaine 0.25% in thoracic PVB in patients undergoing modified radical mastectomy improves the quality and the duration of analgesia and also provides an analgesic sparing effect with no serious side effects.

(Gulbahar et al., 2010)who studied a comparison of epidural and paravertebral catheterization techniques in post-thoracotomy pain management. PVB catheterization can be easily performed and placed in a short span perioperatively. Therefore, it might be the preferred method over TEB which has a high incidence of adverse effects and complication rates.

SUMMARY

Pain after thoracotomy is very severe, probably the most severe pain experienced after surgery. It is also unique as this pain state has multiple implications, including respiratory failure due to splinting; inability to clear secretions by effective coughing, with resulting pneumonia; and facilitation of the often incapacitating chronic pain: the post-thoracotomy pain syndrome. A thoracotomy requires a very painful incision, involving multiple muscle layers, rib resection, and continuous motion as the patient breathes.

Treatment of acute post-thoracotomy pain is particularly important not only to keep the patient comfortable but also to minimize pulmonary complications. Many methods of pain management, each with attendant problems, have been tried with varied success, for example: intercostal nerve block, intrapleural analgesia, cryo-analgesia, lumbar epidural, thoracic epidural, paravertebral block, IV narcotics, intrathecal or epidural narcotics, NSAIDS and transcutaneous nerve stimulation. There are different analgesic modalities for management of post-thoracotomy pain. There are systemic methods which includes infusion and patient-controlled analgesia (PCA) or regional techniques that mainly rely on epidural, intrathecal or paravertebral blocks. Other techniques range from intercostal nerve block to cryoprobeneurolysis .

Intercostal nerve blockade is used routinely at some centers either by single injection of local anesthetics in multiple intercostal nerves before closure of thoracotomy incision or catheter infusion. However, single-shot intercostal nerve blocks with local anesthetic generally do not provide effective long-term analgesia and frequently have to be repeated.

The thoracic paravertebral block is another technique for management of post-thoracotomy pain by injecting local anesthetic in the vicinity of the thoracic spinal nerves emerging from the intervertebral foramen with the resultant ipsilateral somatic and sympathetic nerve blockade. The resultant anesthesia or analgesia is conceptually similar to a "unilateral" epidural anesthesia.

The addition of adjunctive analgesics, such as fentanyl and clonidine, to local anesthetics has been shown to enhance the quality and duration of sensory neural blockades, and decrease the dose of local anesthetic and supplemental analgesia.

Dexmedetomidine is a highly selective α2-adrenorceptor agonist recently introduced to anesthesia; it produces a dose-dependent sedation, anxiolysis, and analgesia (involving spinal and supraspinal sites) without respiratory depression.

Aim of the study: The aim of this study was to evaluate efficacy of both continuous intercostal nerve block and continuous thoracic paravertebral block with or without dexmedetomidine on postoperative analgesia, respiratory functions and stress response for surgery in patients undergoing thoracotomy.

Results: Current study showed significant differences between the four groups as regards VAS at coughing recorded at 2h, 4hrs, 8hrs, 12hrs and 24hrs. As regards respiratory functions (FEV1, PEFR, FVC) between the four groups, current study showed a significant higher values in TPVB with dexmedetomedine group at PACU, 4hrs, 8hrs, 12hrs and 24hrs while FEV1 8hrs, 12hrs and 24hrs showed non statistically significant difference within or between compared to intercostal group, intercostal group with dexmedetomidine and thoracic paravertebral group

without dexmedetomedine. There were significant differences as regard blood cortisol level at4hrs after extubation. Also there were significant differences as regard pain rescue analgesia at 4hrs, 8hrs, 12hrs and 24hrs. As regard hemodynamics (MAP, HR) there was high significant difference between the four groups in the favor of TPV with dexmedetomedine group at PACU, 2hrs, 4hrs, 8hrs,12hrs and 24hrs.As regard respiratory parameters (RR, SPO2, ABG) there was a high statistically difference in the favor of TPVB with dexmedetomidine at 2hrs, 4hrs, 8hrs, 12hrs and 24hrs.

Conclusion: We recommend that the continuous TPVB with dexmedetomidine is safe and effectivemethod in management of post-thoracotomy pain and should be always considered as a continuous intercostal block alternative.

Conclusion

Continuous intercostal nerve block (INB) and Continuous thoracic paravertebral nerve block (TPVB) methods, being one of the components of the analgesia strategy, are quite effective techniques in managing the postthoracotomy pain. There was statistically significant difference in the two methods in terms of efficient analgesia, respiratory functions and stress response to surgeryin favor of TPVB which showed greater analgesic, more improvement of respiratory function, more hemodynamic and respiratory stability than intercostal block especially after adding dexmedetomedine in patients having thoracotomy. We recommend that the TPVB with dexmedetomedine is safe and effective and should be always considered as an intercostal nerve block alternative.

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الملخص العربى

يعد ألم ما بعد عمليات الشق الصدرى أشد انواع الألم الذى يحدث بعد العمليات الجراحية والذى ينتج عنه الكثير من المضاعفات كالفشل التنفسى الناتج عن عدم المقدرة على طرد الافرازات عن طريق السعال والذى يؤدى الى الالتهاب الرئوى هذا بالاضافة الى متلازمة الألم ما بعد الشق الصدرىز

تتطلب عمليات الشق الصدرى شق صدرى مؤلم والذى يشمل العديد من طبقات العضلات, تباعد عظام القفص الصدرى بالاضافة الى الحركة المستمرة الناتجة عن تنفس المريض.

لهذا يعد علاج متلازمة الألم ما بعد الشق الصدرى مهم جدا وذلك لراحة المريض و تقليل المضاعفات التنفسية.

هناك العديد من الطرق المستخدمة للسيطرة على الألم والتى اثبتت النجاح بدرجات متفاوتة على سبيل المثال: الحقن بين الضلوع, الحقن فى الغشاء البللورى, الحقن خارج الأم الجافية فى المنطقة القطنية والصدرية, الحقن بجانب الفقرات الصدرية, المسكنات الوريدية.

هناك العديد من الطرق التى تشمل المسكنات النظامية او المسكنات الموضعية.

الحقن بين الضلوع يستخدم بطريقة روتينية فى بعض المراكز سواء بحقنة واحدة أو بتكرار الحقن بعد قفل جرح الشق الصدرى أو عن طريق الحقن المستمر خلال القسطرة ولكن الحقن مرة واحدة بين الضلوع ليس بالوسيلة الفعالة لتسكين الألم لفترة طويلة مما يتطلب اعادة الحقن غالبا.

الحقن بجانب الفقرات الصدرية هو وسيلة أخرى لتسكين ألم ما بعد عمليات الشق الصدرى و الذى يحقن فيه العقار خلال أعصاب العمود الفقرى التى تبرز من فتحات ما بين الفقرات والتى توازى تسكين الألم الناتج عن الحقن خارج اللأم الجافية.

وقد أظهر اضافة العقاقير المسكنة للمخدرات الموضعية مثل عقار الفنتانيل و عقار الكلونيدين تحسن فى كفاءة ومدة تسكين الألم بالاضافة الى تقليل جرعات المخدرات الموضعية و المسكنات الجهازية.

يعتبر عقار الديكسميديتوميدين ناهض انتقائى عالى لمستقبلات ألفا-2 والذى دخل مؤخرا الى عالم التخدير و يؤدى هذا العقار الى تسكين الألم بالاضافة الى السكون و تهدئة الأعصاب بدون التسبب فى الفشل التنفسى.

الهدف من الدراسة:

تقييم تأثير كل من الحقن المستمر بين الضلوع والحقن المستمر جانب الفقرات الصدرية سواء باضافة أو بدون اضافة عقار الديكسميديتوميدين على تسكين الألم, الوظائف التنفسية و الاستجابة العصبية لمرضى عمليات الشق الصدرى.

النتائج:

أوضحت هذه الدراسة اختلافات كبيرة بين الأربع مجموعات فيما يتعلق بدرجات قياس الألم البصرى بالمجهود و الذى تم تسجيله عند ساعتين, اربع ساعات, تمان ساعات, اثنى عشرة ساعة و اربع وعشرين ساعة بعد العملية.

وفيما يتعلق بالوظائف التنفسية أوضحتالمقارنة بين اللأرع مجموعات فى هذه الدراسة فرق كبير لصالح مجموعة الحقن بجانب الفقرات الصدرية المضاف اليه عقار الديكسميديتوميدين والتى تم قياسها عند دخول المريض عناية ما بعد العمليات الجراحية عند أربع ساعات, ثمان ساعات, اثنى عشرة ساعة و أربع و عشرين ساعة.

فيما يخص الاستجابة العصبية للعمليات الجراحية و مستوى الكورتيزول فى الدم فقد كان هناك فرق واضح لمستوى الكورتيزول بعد أربع ساعات من ازالة الأنبوبة الحنجرية لصالح مجموعة الحقن المستمر بين الفقرات الصدرية المضاف اليه عقار الديكسميديتوميدين.

بالنسبة لاستهلاك المسكنات بعد العملية فأيضا كان هناك فرق واضح بعد مقارنة الأربع مجموعات لصالح مجموعة الحقن بين الفقرات الصدرية المضاف اليه عقار الديكسميديتوميدين هذه المجموعة التى استهلكت أقل كمية من المسكنات الجهازية بعد العملية.

الاستنتاج:

ننصح باستخدام الحقن المستمر بين الفقرات الصدرية المضاف اليه عقار الديكسميديتوميدين والذى أظهر كفاءة و أمان فى علاج متلازمة الألم ما بعد عمليات الشق الصدرى.