

DISSERTATION ON PLEURAL ANALGESIA FOR POSTOPERATIVE PAIN RELIEF.

This Dissertation is submitted to

**The Tamilnadu Dr.M.G.R. Medical University, Chennai
for partial fulfillment of requirement for the award of
M.D.degree – branch X in ANAESTHESIOLOGY,
Govt. Madras Medical College & Hospital, Chennai**



**THE TAMILNADU DR.M.G.R. MEDICAL UNIVERSITY
CHENNAI - TAMILNADU**

MARCH 2008

CERTIFICATE

This is to certify that this dissertation entitled **“Efficacy of interpleural analgesia in reducing postoperative pain and parenteral analgesic requirement in patients undergoing upper abdominal surgery”** is a bonafide original work of **Dr. R.Padmini** in partial fulfillment of the requirement for **M.D. (Branch X) anaesthesiology** examination of the Tamil Nadu Dr.MGR Medical University to be held in March 2008

Dr.T.P.Kalaniti.M.D
Dean
Govt. Madras Medical College
and Hospital
Chennai - 3.

Prof..S.Gayathri.M.D.D.A
Head of the Department
Department of anaesthesiology
Govt.Madras Medical college
Hospital
Chennai-3

Place: Chennai

Date: March 2008

ACKNOWLEDGMENT

I profusely thank **Dr.T.P.Kalaniti, M.D.**, Dean, Madras Medical college, Chennai, who permitted to pursue research work and to utilize the case material.

I express my sincere gratitude to my chief, **Prof. S.Gayathri,M.D,D.A.**Head of the Department of Anaesthesiology, for her keen interest, constant encouragement, guidance and valuable suggestions throughout this study.

I am deeply indebted to Dr.GanapathyAsokan,M.D,D.A. Associate professor of anaesthesiology for his valuable suggestion and guidance through out the course of the study.

I express my deep gratitude to Dr.T.Venkatachalam M.D,D.A . Registrar for his valuable guidance and support throughout the study. My sincere thanks to my assistant professors and colleagues in my department for their support.

I am extremely thankful to Mr. A.S.Tholkapian, ICMR for analyzing the results.

Last but not the least, my heartiest and humble gratitude to the patients who were kind enough and helpful during the study.

CONTENTS

S.NO	TITLE	PAGE
1	INTRODUCTION	1
2	AIM OF THE STUDY	3
3	PHYSIOLOGY	4
4	REVIEW OF LITERATURE	11
5	ANATOMY	15
6	DRUGS	28
7	PATIENTS AND METHODS	37
8	RESULTS	41
9	DISCUSSION	49
10	CONCLUSION	52
11	REFERENCES	53

INTRODUCTION

Surgery produces both visceral and somatic pain. This results in the release of nociceptive substances such as prostaglandins, histamine, serotonin, bradykinin, 5-hydroxytryptamine, substance P and generation of noxious stimuli that are transduced by nociceptors and transmitted by A delta and C nerve fibres to the neuraxis.

Pain is the most important factor responsible for ineffective ventilation, ineffective cough, and impaired ability to sigh and breathe deeply, in patients after upper abdominal surgery. This may contribute to pulmonary atelectasis leading to ventilation/perfusion abnormalities and hypoxemia, as well as infection, after surgery .

Many of these adverse effects can be eliminated or reduced by adequate post operative pain relief. Several methods have been advocated to reduce postoperative pain.

The administration of local anesthetics into the pleural space is a technique of providing analgesia of rapid onset and long duration. This analgesia is accomplished without causing the respiratory depression or sedation associated with the use of opioids.

This study is chosen to investigate the efficacy of interpleural analgesia in treating postoperative pain .

AIM OF THE STUDY:

This study intends to prospectively analyze the efficacy of interpleural analgesia in reducing post operative pain and parenteral analgesic requirement in patients undergoing upper abdominal surgery.

PHYSIOLOGY OF PAIN

Pain impulses from most of the abdominal and thoracic viscera are conducted through afferent fibers that travel with the sympathetic nervous system. Impulses from structures deep in the pelvis are transmitted via the sacral parasympathetic nerves.

Pain receptors in the viscera are similar to those in the skin but more sparsely distributed. Any event that causes stimulation of nerve endings in the viscera produces diffuse, poorly localized pain and often associated with nausea and signs of autonomic nervous system activation.

Visceral pain typically radiates and may be referred to surface areas of the body with the same dermatomal origin. Visceral pain initiates reflex contraction of the nearby skeletal muscles which make the abdominal wall rigid when the inflammatory processes involve the peritoneum.

Somatic pain is described as sharp, stabbing, well localized pain that typically arises from the skin, skeletal muscles and peritoneum. Pain from surgical incision and peritoneal irritation is somatic pain. This pain is transmitted via the spinal nerves.

Further transmission is determined by complex modulating influences in the spinal cord. Some impulses pass to the anterior and anterolateral horns to provoke segmental reflex responses. Others are transmitted to higher centers via the spinothalamic and spinoreticular tracts, where they produce suprasegmental and cortical responses.

Factors affecting clinical pain.

There are many factors affecting the variability of clinical pain complaint, behaviours and response to management. These include biological factors, psychological factors ,social/ environmental factors pharmacological factors .

Biological factors.

1. Sensitization of peripheral and central nociceptors in response to prolonged noxious stimuli so amplifying the subsequent response.
2. Modulation or dampening of nociceptors at various points of their passage to consciousness.
3. Eliciting motor or autonomic reflexes

Psychological factors

1. Affective : emotional response to pain is influenced by preexisting affective dysfunction and personality traits
2. Cognitive : Understanding the nature, cause, purpose and consequences of the pain, together with learned influences .

Social and environmental factors

The gain derived from an individual's interaction with family, work, community and health carers together with immediate context.

Pharmacological factors

Individual's pharmacokinetic and pharmacodynamics variability.

Effects of postoperative pain on various systems.**Effects on respiratory system.**

Surgery involving upper abdomen and thorax produce number of pulmonary changes. They include reduced vital capacity, tidal volume, residual volume, functional residual capacity and forced expiratory volume. The greatest reduction is in the total lung capacity. Decrease in forced vital capacity upto 50% on first day of abdominal surgery.

Surgical incision involving the upper abdomen decreases the diaphragmatic function resulting in reduced pulmonary compliance, muscle splinting, inability to breathe deeply or cough forcefully and in some cases may even cause hypoxemia and hypercarbia. Surgeries involving lower abdomen may cause less marked effect on respiration.

Effects on cardiovascular system.

Pain causes sympathetic stimulation resulting in tachycardia, increased stroke volume, increased cardiac work and increased myocardial oxygen consumption. This coupled with hypoxemia results in increased risk of myocardial ischemia or infarction in potential subjects. Also decreased ambulation due to pain leads to venous stasis, increased risk of deep vein thrombosis and pulmonary embolism.

Effects on Neuroendocrine and metabolism

A lot of effort is being taken to reduce the stress response during surgery. But post operative pain leads to suprasegmental reflex response resulting in hypothalamic stimulation, increased sympathetic tone ,an increased catecholamine and catabolic hormone secretion (ACTH, ADH, Glucagon, CAMP, Renin, Angiotensin II) and decreased anabolic hormones like insulin. These responses collectively result in sodium and water retention, hypoglycemia and increased free fatty acid levels, ketones and lactate. This is further worsened by reflex muscle spasm causing increased oxygen demand and lactate production. Thus a catabolic state and negative nitrogen balance ensues.

Effects on Gastrointestinal system and urinary system.

Pain causes paralytic ileus, nausea, vomiting and urinary retention. Severe postoperative pain causes increased morbidity and mortality. Effective analgesia results in decreased incidence of respiratory complications, decreased incidence of cardiovascular complications, early return of GIT activity, early ambulation and early discharge from the hospital.

Postoperative pain relief is necessary for patient comfort, and to facilitate ventilation and ambulation. Upper abdominal surgery, including cholecystectomy, induces alterations of pulmonary function. Parenteral opioids which are used extensively for postoperative analgesia are associated with undesirable side effects. These include hypoxic episodes while the patient is asleep and incomplete and sporadic analgesia. The use of opioid analgesia, either intravenously, intramuscularly, or intraspinally can cause respiratory depression.

Methods of postoperative pain relief.

The various methods of post operative pain relief are

A. Opiates

1. Intramuscular
2. Intravenous
3. Intradural/ Extradural
4. Patient controlled analgesia (PCA)
5. Other routes :oral, transmucosal, transdermal and rectal.

B. Non opiates

Invasive

1. Local anaesthesia
2. Regional anaesthesia
3. Cryoanalgesia
4. Continuous intrapleural infusion

Noninvasive

1. Inhalational
2. Transcutaneous electrical nerve stimulation(TENS)
3. Hypnosis
4. Electroacupuncture
5. Relaxational techniques.

REVIEW OF LITERATURE

Interpleural instillation of local anaesthetic solutions was originally described in 1984 by Kvalheim and Reiestad (1) for postoperative pain relief. Since then, interpleural analgesia has been shown to be effective for postoperative pain management in patients undergoing cholecystectomy, breast surgery, and renal surgery with remarkably low blood levels of local anaesthetic achieved. (2-4)

Rocco and Reiestad have shown the efficacy of interpleural analgesia in patients with multiple rib fractures and flail chest(5). Reiestad and Kvalheim found the technique effective in treating severe acute and subacute thoracic herpes zoster, perhaps even preventing the development of chronic post-herpetic neuralgia.(6) Recently the interpleural catheter technique has been shown to be effective in the treatment of various chronic pain conditions.(7,8)

Interpleural analgesia produces regional analgesia of the chest wall and is used for pain therapy of different indications which include breast, renal, gall bladder and thoracic surgery, and chronic pain(9).

The effect of interpleural analgesia on postoperative hospital course was analyzed in a prospective randomized study by Frank et al (10) of patients undergoing cholecystectomy .

In their study, control patients were treated in the standard manner with systemic narcotics alone; catheter patients had an interpleural catheter placed at the end of surgery and, in addition, could receive systemic narcotics if necessary. Pain score, pulmonary function and narcotic requirement were measured over the first postoperative day. Catheter patients had a lower average pain score (visual analog scale (VAS), 3.6 versus 5.2), decreased narcotic requirement in the recovery room and improved oxygen saturation (96% versus 93%). However, there was no statistical difference in amount of morphine (catheter, 25 ± 14 mg; control, 31 ± 15 mg), number of narcotic injections.

In another study by Luc Frenette et al (11) Forty-two patients undergoing elective cholecystectomy were randomly assigned to two groups: one to receive interpleural administration of bupivacaine-adrenaline mixture (Group I = 22 patients) and the other standard administration of intramuscular meperidine (Group 2 = 20 patients) for postoperative pain relief. This study concluded that the interpleural

analgesia can achieve better pain relief with greater ventilatory capacity than a standard analgesic regimen in the first two days after surgery.

In a double-blind, randomized control trial comparing intraperitoneal versus interpleural morphine or bupivacaine for pain after laparoscopic cholecystectomy by Schulte et al(12), interpleural bupivacaine (0.25%) produces adequate analgesia after laparoscopic cholecystectomy. the lack of effect of intraperitoneal injections was attributed to the small dose and to a rapid dilution within the peritoneal cavity. Interpleural morphine (0.005%) group was ineffective due to an intact perineurial barrier in the noninflamed pleural cavity, which restricts the transperineural passage of morphine to opioid receptors on intercostal nerves.

In the current literature there are publications providing evidence both supporting and opposing the effectiveness of the postoperative pain management via IP analgesia after thoracotomy. An explanation for insufficient pain reduction may be the loss of local anesthetics in the chest tubes and altered diffusion within the parietal pleura after mechanical irritation by the surgical procedure. A dilution of the local anesthetics by pleural exudation appear to play a subordinate role

because we could not demonstrate a relationship between chest tube fluid loss and analgesic requirement or pain scores.

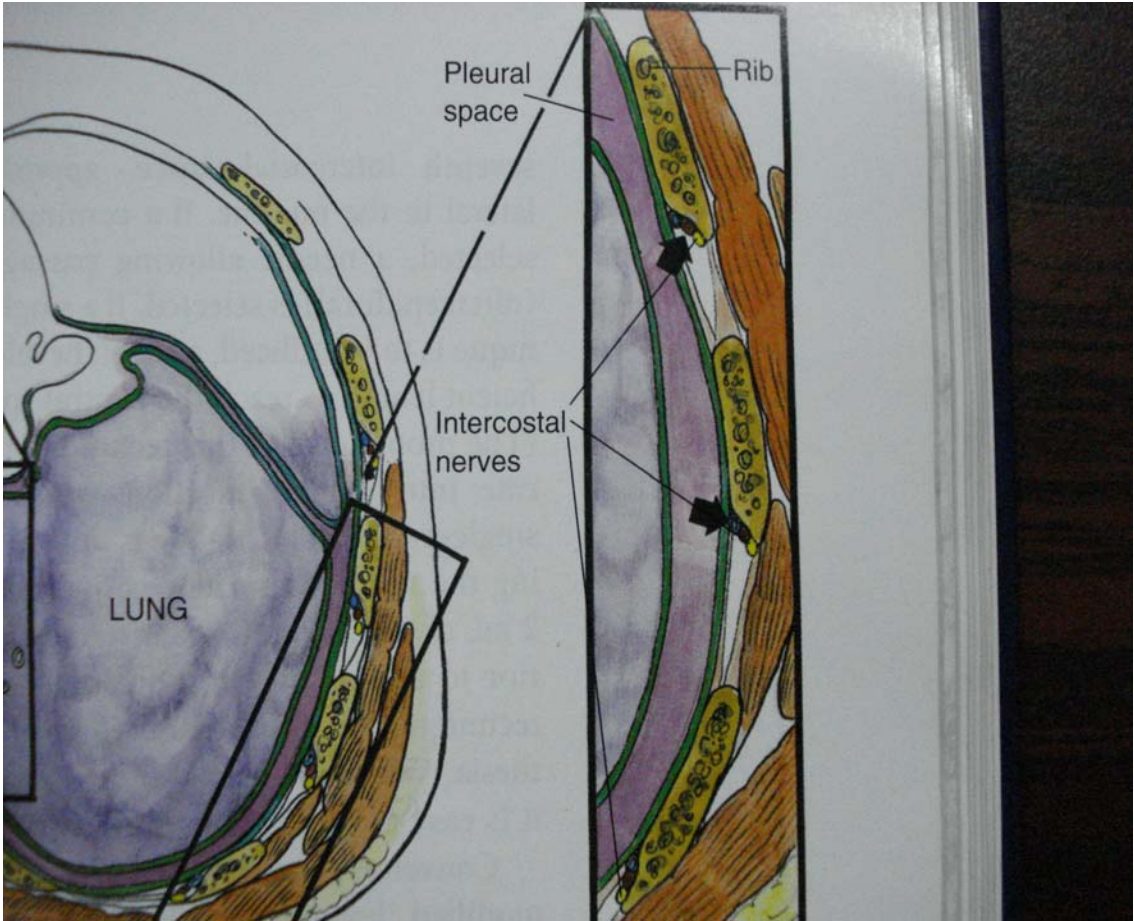
Anatomy of pleural cavity

Each lung is covered with a smooth glistening layer of visceral pleura except on the medial surface where the structures in the root of the lung are continuous with the mediastinum. Here the visceral pleura which surrounds the root is continuous with the parietal pleura which covers the surface of the mediastinum (mediastinal pleura). The pleura which surrounds the root of the lung extends inferiorly as a narrow fold called pulmonary ligament.

The mediastinal pleura is continuous with the other parts of the parietal pleura.

- (1) Anteriorly and posteriorly with the costal pleura which lines the thoracic wall.
- (2) Inferiorly, with diaphragmatic pleura which covers the anterior surface of the diaphragm lateral to the mediastinum.
- (3) Superiorly, with the dome of the pleura which extends through the superior aperture of the thorax into the root of the neck.

Anatomy of pleural space



The diaphragmatic pleura and the dome of the pleura are continuous with the costal pleura respectively at the margins of the diaphragm and the first rib.

The parietal pleura differs from the visceral pleura in having a thick fibrous layer (Endothoracic fascia) externally.

Dome of the pleura

Dome of the pleura bulges into the root of the neck from the interanal margins of the first rib. The right and left dome of pleura are separated by the midline structures (trachea and esophagus) and the blood vessels passing to and from the neck.

The subclavian vessels arch over the anterior surface of the dome, the artery near its highest point and the vein anteroinferior to the artery. The internal thoracic artery descends on the front of the dome from the subclavian artery to the back of the first costal cartilage. Between these two structures and the dome is a layer of dense fascia (Suprapleural membrane) which spreads from the transverse process of seventh cervical vertebra to the internal margin of first rib.

Parenchyma of the lung and visceral pleura are insensitive to pain.

Nevertheless the bronchi and parietal pleura are very sensitive to pain.

Pleural recesses

These are the parts of the pleural cavity which are not occupied by the lung except in full inspiration .

The costamediastinal recess lies along the anterior margin of the pleura.

The costodiaphragmatic recess extends inferiorly between the thoracic wall and the lateral and posterior parts of the diaphragm.

Deep in the recess , where the costal and the diaphragmatic parts unite they are bound down to the costal cartilages and diaphragm by a narrow thickening of endothoracic fascia (phrenicopleural fascia)

The potential space between these two layers is the pleural cavity. Under normal conditions the two surfaces are in opposition except for a small quantity of lymph which acts as a lubricant.

Surface Anatomy

The surface anatomy of pleura is as follows. The apex of the pleura project 2 to 3 cms above the clavicle at the apex of the pleural cavity outer surface is surrounded by loose areolar tissue(Sibsons fascia) in which small fibrous bands can sometimes be demonstrated coursing over the dome of the lung (Bands of Sebalot). From the apex the pleura descends medially meeting in the midline at the second costal space or sternal angle. From the sternal angle pleura descends down till the 4th costal cartilage on both the sides. From here onwards in the right side pleura continues medially till the 6th costal cartilage. In the left side it deviates laterally from the 4th costal cartilage to 6th costal cartilage. On both the sides from the 6th costal cartilage pleura arches laterally and reaching the 8th rib in the midclavicular line, 10th rib in midaxillary line, 12th rib lateral to levator spinae muscle. From here the pleura runs horizontally reaching the posterior midline at the level of T12 spine.

Intrapleural pressure

Owing to the continual retractive force exerted by the elastic recoil of the lung, intrapleural pressure under normal conditions is negative. Elastic recoil of the lung is made up of three factors.

1. The elastic tissue in the bronchial wall and also those coursing through out the interstitial tissue of the lung.

2. The arrangement of the muscle fibres of the bronchioles in a “geodesic” network so that on contraction bronchial tree not only becomes reduced in diameter but also shortened in length

3. The surface tension of the fluid lining the alveolar walls.

Intrapleural pressure ranges from -5.6 mm of Hg on inspiration to -2.6 of Hg on expiration. The pressure is less negative at the bottom than at the top of the lung.

Mechanism

Visceral pain is believed to be transmitted along afferent fibres from the abdominal viscera to the splanchnic nerves and also by the lower intercostal nerves which innervate the peritoneum. The lower intercostal nerves also supply the upper part of the abdominal wall. It is therefore important to block both the lower intercostal and splanchnic nerves in order to relieve postoperative pain.

The intercostal space posteriorly has three layers. The external intercostal muscle, posterior intercostal membrane and the intercostalis intimus muscle. The intercostal nerves lie in between the posterior intercostal membrane and the intercostalis intimus muscle, whereas posterior intercostal membrane forms a complete barrier beneath the external intercostal muscle, the intercostalis intimus muscle is incomplete and freely allows fluid to pass in to the sub pleural space. Thus, interpleural analgesia can be accomplished by placing a catheter tip either deep to the internal intercostal muscle but superficial to the parietal pleura or between the parietal and visceral layers of pleura with concomitant multiple segmental intercostal nerve block.

The number of nerves affected depends on

1. The level of the catheter
2. The volume of anaesthetic injected
3. Effects of gravity.

Diffusion of local anaesthetic from the pleural space seems to block several intercostal nerves simultaneously. The local anaesthetic is also believed to diffuse easily through the parietal pleural and this effectively blocks most of the intrathoracic sympathetic chain including the splanchnic nerves. The blockade of both somatic and visceral pain fibres in interpleural block is an important distinction when compared with coeliac plexus block.

Techniques

The "**open chest**" technique consists of insertion of an epidural type catheter via an epidural needle posterior and superior to the incision, the catheter being sutured at the skin, bacterial filter attached and sterile dressing applied. Infusion of the drug are not very effective with this method due to loss of injected drug through chest drain tube. It will not be possible to clamp the chest drain for any length of time because of risk of pneumothorax in patients with an air leak.

In the "**closed chest**" technique a Tuohy needle and lubricated glass syringe are used. The needle is inserted at the sixth intercostal space, in the posterior axillary line, and walked off the superior border of the rib with its bevel directed towards the parietal pleura and its shaft parallel to the posterior path of the rib. Negative intrathoracic pressure causes sudden, dramatic loss of resistance, sucking the plunger of the syringe down as parietal pleura is traversed. The syringe is then removed, with the thumb preventing further air entrainment and the catheter is advanced 6-10 cm.

Contraindications

1. Pleural Effusion
2. Pleural Adhesions and fibrosis
3. Injuries
4. Bullous Emphysema
5. Local infection
6. Bleeding diathesis
7. Recent pneumonia or pleuritis
8. Cardiac arrhythmias
9. Convulsions
10. Allergy to local anesthetics.

Complications

Pneumothorax is a significant risk. Unilateral sympathetic block may be observed and can result in Horner's syndrome. Chest wall hematoma is a possibility. Systemic absorption with significantly high plasma concentrations of local anaesthetics can be observed with continuous infusions. Lung injury with laceration or bronchopleural fistula formation are possible. Rarely local anaesthetic can spread to the epidural space and left recurrent laryngeal nerve palsy has been reported(13).

Brismar (14) reported that four of 21 patients developed pneumothorax and one patient had the catheter placed extrapleurally. Seltzer et al (15) reported one case of seizure with a measured blood concentration of bupivacaine of 4.9 ng / ml at 5 min after injection.

Clinical assessment of pain

Postoperative pain severity can be scored and recorded .Pain severity scores cannot be viewed in isolation .They should be considered along with traditional ward observations of pulse rate, blood pressure and respiratory rate .Such recording most likely to improve the safety and effectiveness of pain management.

The simple pain scoring systems are

1. Categorical rating scales(CRS)

Frquently used to assess postoperative pain because it is easy verbal method that can employ different descriptors of pain.

e.g –No pain, mild pain, moderate pain, severe pain.

2. Visual analogue scale (VAS)

Employs 10 cm drawn line with the left anchor point descriptor labeled “No pain” and right sided equivalent labelled “worst possible pain”

3. Verbal numerical rating scale (VNRS)

Patients are asked to estimate their pain severity as a number “0” being no pain, and “10” being worst possible pain.

Visual analogue scale (VAS)

The VAS is a simple and sensitive assessment that is often used to measure and study a patient's pain. Its usefulness has been validated by several investigators. A VAS has been found to be superior to fixed interval scales, relative pain scales, and verbal reports of pain. Subjects simply place a mark on a 10cm line anchored with the terms describing the extremes of pain intensity. It is often used in the immediate post-operative period to determine the effects of analgesics and/or pain management regimens.

The VAS had been adapted for pediatric populations by substitution

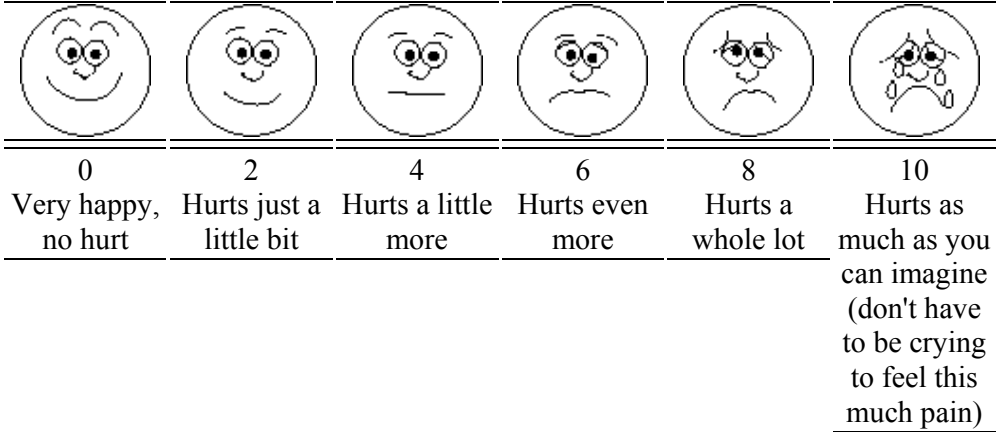
—————										
0	1	2	3	4	5	6	7	8	9	10
No pain										Worst pain imaginable

pictures of faces ranging from agony to happiness and is termed the

Faces Pain Scale.

Categorical Scale			
None (0)	Mild (1-3)	Moderate (4-6)	Severe (7-10)

Pain Faces Scale



--

Drugs

Pentazocine

Pentazocine is a benzomorphan derivative that possesses opioid agonist as well as weak antagonist action. It is presumed to exert its effects at delta and Kappa receptors.

Pharmacokinetics

Pentazocine is well absorbed after oral or parenteral administration. First pass hepatic metabolism is extensive. Oxidation of the terminal methyl groups results in inactive glucuronide conjugates which are excreted in the urine. Up to 25% of the administered dose excreted unchanged in urine. Elimination half time is 2 to 3 hours.

Dose

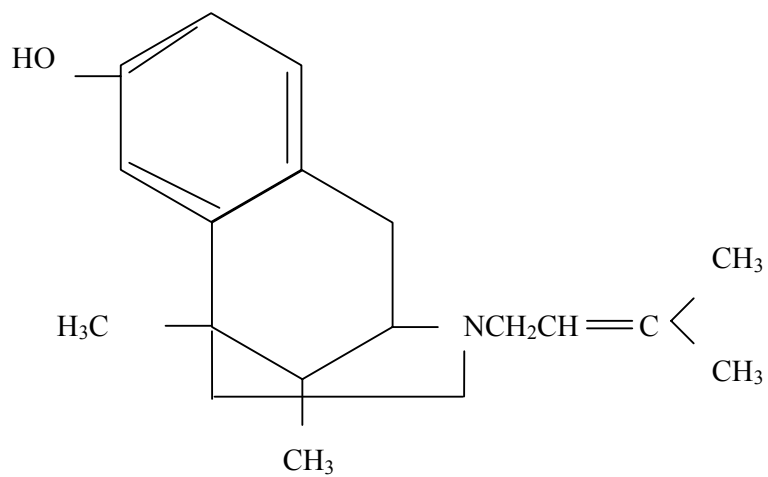
Pentazocine 10 to 30 mg IV or 50 mg orally is used most often for relief of pain.

Side effects

Most common side effects of pentazocine is sedation, diaphoresis and dizziness. Nausea and vomiting are less common. It

produces increase in the plasma concentrations of the catecholamines ,which may account for increases in the heart rate,blood pressure pulmonary artery pressure and left ventricular end diastolic pressure.

The increase in biliary tract pressure is least common with pentazocine. Increasing the parenteral dose does not increase the ventilatory depression.

Structural Formula - PENTAZOCINE

Bupivacaine

This belongs to amide group of local anaesthetics which contain asymmetric carbon atom.

Mechanism of action

Bupivacaine binds to sodium channels in the inactivated –closed state resulting in inhibition of sodium permeability and hence conduction of nerve impulses in the form of propagated action potential cannot occur.

Pharmacokinetics

Absorption of bupivacaine from its site of injection in to systemic circulation is influenced by site of injection and dosage, use of epinephrine and pharmacological characteristics of the drug.

After rapid entry of bupivacaine in to venous circulation pulmonary extraction occurs which limits the concentration of the drug reaching the systemic circulation. In addition to the tissue blood flow and lipid solubility of the drug, the patient related factors such as age cardiovascular status and hepatic function will also influence the absorption and resultant plasma concentration .Protein binding of the drug will influence the distribution and excretion .Clearance values and

elimination half times represent mainly the hepatic metabolism, because renal excretion of unchanged drug is minimal ($< 5\%$).

Dose

2mg/kg upto maximum of 175 mg .Duration lasts upto 240 to 480 minutes. 95% of the drug is bound to the alpha 1 acid glycoprotein in the plasma. Volume of distribution is 73 litres. It is metabolized by the aromatic hydroxylation, N-dealkylation, amide hydrolysis and conjugation. Clearance rate is 0.47litres /Min. The measured total urinary excretion of bupivacaine and its dealkylation and hydroxylation metabolites account for more than 40% of the total anaesthetic dose.

Side effects

Allergic reactions are less common than the ester group of local analgesics. Important complications include systemic toxicity which depends on

1. Dose
2. Vascularity of injection site.
3. Presence of epinephrine
4. Physiochemical properties

CNS Toxicity

Low concentration is characterized by numbness of the tongue and circumoral areas. As the plasma concentration continues to increase bupivacaine readily crosses the blood brain barrier and produce predictable pattern of CNS change. Restlessness, tinnitus, vertigo occur initially. Further increase in CNS concentration results in slurred speech and twitching .Finally tonic clonic seizures occurs which is classically followed by hypotension and apnea. The onset of seizures may reflect selective depression of inhibitory cortical neurons by local anaesthetic leaving excitatory pathways unopposed.

The typical plasma concentration of bupivacaine associated with seizures is 4.5 to 5.5 microgram/ml.

Treatment of Seizures include ventilation of patients lung with oxygen to prevent arterial hypoxemia and metabolic acidosis. Delivery of supplemental oxygen at the earliest sign of local anaesthetic toxicity is equally important. Intravenous administration of benzodiazepine is effective in suppressing local anaesthetic induced seizures.

CVS toxicity

Accidental intravenous injection of bupivacaine may result in precipitous hypotension cardiac dysarrhythmia and atrioventricular block. It is due to prolonged blockade of cardiac sodium channels .The threshold for cardiotoxicity produced by bupivacaine may be decreased in patients treated with drugs such as beta adrenergic blockers, digitalis, calcium channel blockers .This suggests that bupivacaine should be used with caution when concomitant cardiac medications known to depress the myocardial impulse propagation.

Epinephrine and phenylephrine may increase bupivacaine cardiotoxicity owing to inhibition of cyclic CAMP production. Dissociation of highly lipid soluble bupivacaine from sodium channel receptors site is slow, accounting for the drugs persistent cardiac depression. Tachycardia can enhance frequency dependent blockade of cardiac sodium channels by bupivacaine. The plasma concentration of bupivacaine associated with cardiovascular toxicity is 8 to 10 microgram/ml.

Treatment

It consists of intravenous administration of bretylium 20 mg/kg which reverses bupivacaine induced cardiac depression and increases the threshold for ventricular tachycardia.

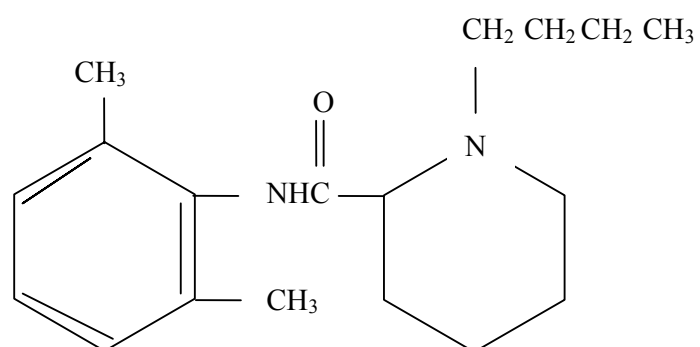
Ventilatory response to hypoxia

Unlike other local anaesthetics systemic absorption of bupivacaine such as following peripheral nerve block stimulates the ventilatory response to carbondioxide.

Preparations

0.5% solution 20 ml vial with sodium metabisulphite as preservative.

0.5 % solution 4 ml ampoule without preservative for intrathecal use.

BUPIVACAINE STRUCTURE

PATIENTS AND METHODS

After approval from local ethics committee and written informed consent 36 patients undergoing elective upper abdominal surgeries like open cholecystectomy, nephrectomy , pyelolithotomy and pyeloplasty at Government General Hospital, Chennai were enrolled in the study. The inclusion criteria were age 19 to 65 years ASA physical status 1 & 2 with no contraindications for the technique and drugs. These include pleural injury, pleural adhesion, fibrosis or effusion, COPD, local infection, bleeding diathesis and allergy to study drugs. The linear visual analog scales (VAS) were explained to the patients prior to the study.

Patients were premedicated with Inj glycopyrrolate 0.2mg and Inj fentanyl 100 micrograms IV just before induction. Patients were induced with Inj propofol 2mg /Kg, Inj Suxamethonium 100mg IV and intubated one minute later with appropriate size endotracheal tube orally. The anaesthesia was maintained with nitrous oxide – oxygen mixture 3:2, muscle relaxant Inj Vecuronium and volatile agents.

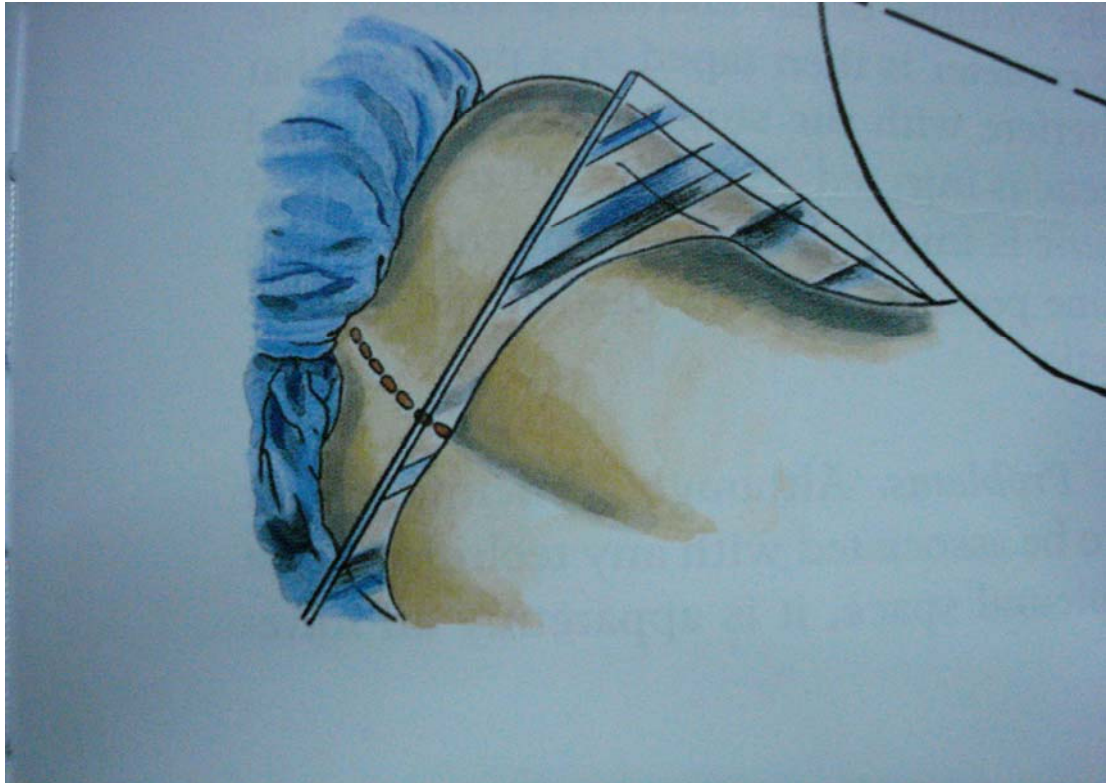
When the surgery was over the patients were randomly assigned to two treatment groups of 18 patients in each.

- 1) Pleural analgesia (bupivacaine) combined with Parenteral analgesics (Pentazocine).
- 2) Parenteral analgesics alone. (Pentazocine)

In patient assigned in pleural group the catheter was inserted unilaterally on the side of incision. The patients were positioned laterally with operative site up and pleural catheter was inserted at the sixth intercostal space in the posterior axillary line just before anaesthesia was discontinued during spontaneous ventilation. Intercostal drainage tube was kept ready throughout the study period to manage any untoward pneumothorax occurrence..

Under aseptic precautions the 17 G Tuohy needle loaded with 5ml syringe containing normal saline introduced in the sixth intercostal space and then walked off the superior edge of the rib. The loss of resistance to saline technique was used to identify the entry in to the pleural cavity. The catheter was then advanced posterosuperiorly past the tip of the needle and fixed in position close to the paravertebral space and the

Position for interpleural block



needle is withdrawn. Forty milliliters of Injection bupivacaine 0.25%, was injected through catheter after negative aspiration for blood. Patient was turned supine and after reversal extubated.

In patients in control group no analgesics were given before extubation.

One hour after extubation and every 6 hrs thereafter in both the groups pain was recorded using Visual analog scale (VAS). The patients were given pain relief medication on demand . In the control group patients were given Inj Pentazocine 30 mg intramuscularly .In the pleural group break through pain was treated similiarly.

Postoperatively, one hour after pleural puncture chest radiograph was obtained for detection of a possible pneumothorax in pleural group. Pain was evaluated with a 10 cm VAS in both the groups. Patients were continuously monitored with ECG. Blood pressure and heart rate were recorded noninvasively every 5 minutes up to 30 minutes after the bolus in both groups.

The total parenteral analgesic requirement in the initial 48 hrs postoperative period was recorded. The study was stopped after 48 hours because of concerns of the interpleural catheter displacement following mobilization of the patient and fear of catheter-related infection.

Statistical Analysis

Student t test was used to compare the pentazocine requirement and VAS scores between the pleural and control groups.

Data was analyzed with SPSS software.

Data are presented as means \pm SD. The P values were provided to indicate statistical significance. $P < 0.05$ was considered as significant.

RESULTS

One patient was excluded from the study due to aspiration of blood in the pleural catheter. Demographic data were similar in both the groups (Table 1). Mean age was $40.7\text{yrs} \pm 11.30$ (21 to 56 yrs) in pleural group and $44.6\text{ yrs} \pm 11.9$ (18 to 65 yrs) in control group. No episodes of hypotension or bradycardia were noted. Neither pneumothorax nor CNS (central nervous system) toxic reactions (tremor, perioral numbness, muscle twitches, metallic taste, tinnitus, convulsions) were noted. The catheter insertion using loss of resistance technique described above was easy to identify the pleural space and effective.

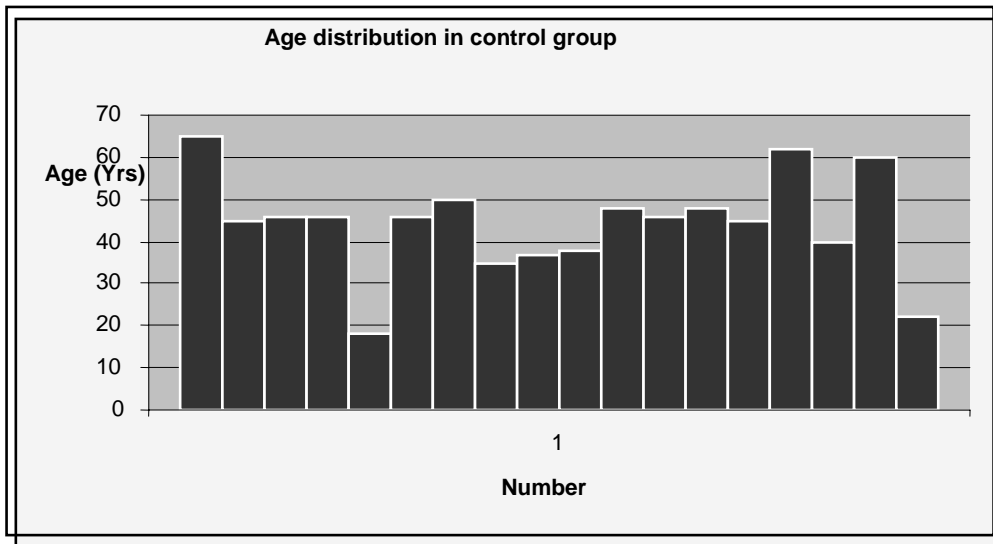
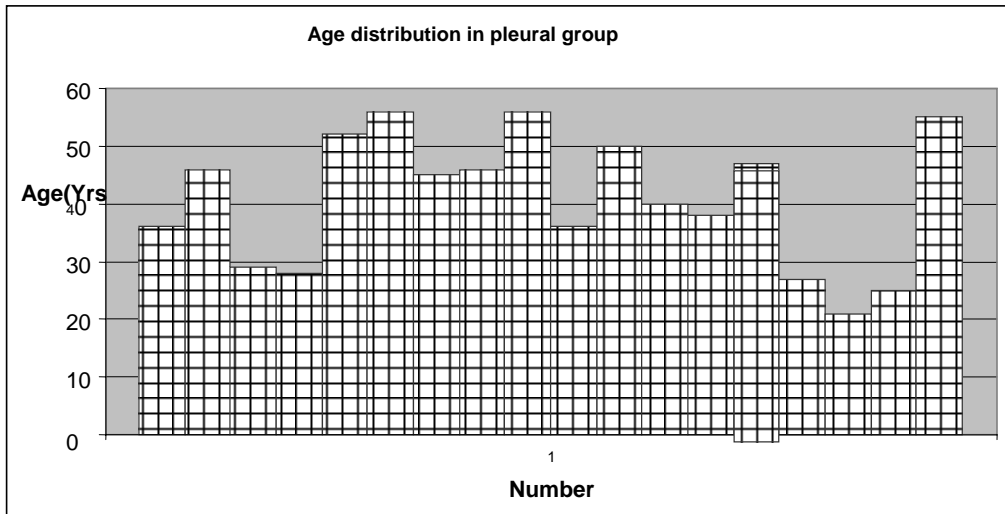
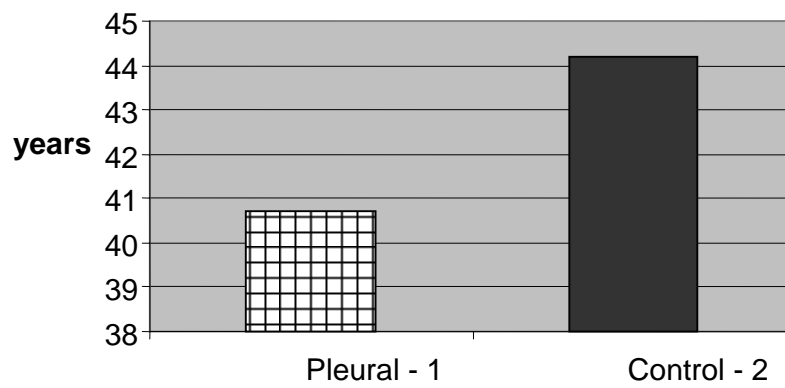


Table 1: Patient characteristics

	Pleural Group(18)	Control group(18)
Age(yr)	40.7 ± 11.3	44.2 ± 11.9
Sex(male/female)	5/12	10/8
Weight(Kg)	55.4 ± 5.9	57 ± 6.8

Age characteristics

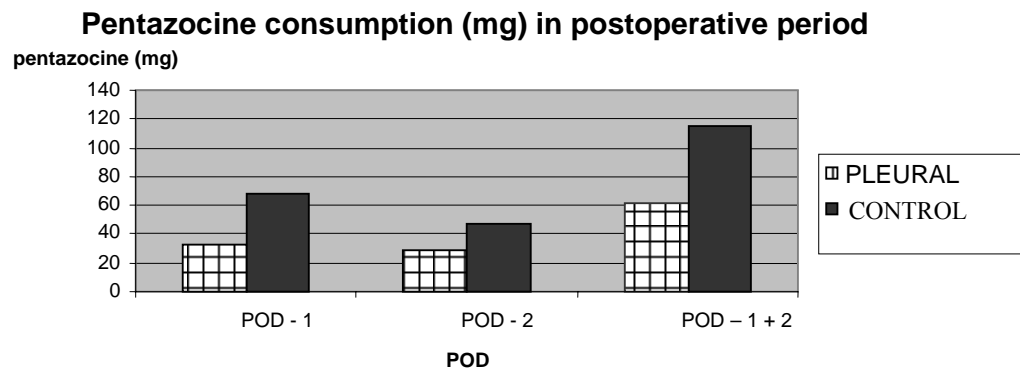


The consumption of pentazocine (table 2) was analyzed. Daily consumptions of pentazocine were higher in control group than in pleural group, for Day 1 ($P < 0.001$), Day 2 ($P < 0.01$) and Day1 + 2 ($P < 0.001$) and was significant. It was found that difference was more significant on Day 1. Patients of control group received a mean dose of 114.9 ± 20.7 mg of pentazocine in the first 48 hrs postoperatively in contrast to pleural group which received mean dose of 61.6 ± 8.7 mg.

Table 2: Pentazocine consumption (mg) in the two groups recorded at Days 1 and 2 postoperatively and during whole study period (Day 1 + Day 2)

Group	Day1	Day 2	Day1+ 2
Pleural	33.3 ± 9.7	28.3 ± 7.0	61.6 ± 8.7
Control	68.3 ± 13.8	46.6 ± 21.1	114.9 ± 20.7
P Value	< 0.001	< 0.01	< 0.001

**BAR DIAGRAM SHOWING PENTAZOCINE CONSUMPTION
IN PLEURAL & CONTROL GROUP**



Mean pain scores were significantly reduced 30 min after IP instillation of bupivacaine 0.25 % compared to control group . The mean pain score of the pleural group is 2.96 ± 0.72 and mean pain score of the control group is 6.04 ± 1.30 for 48 hrs.

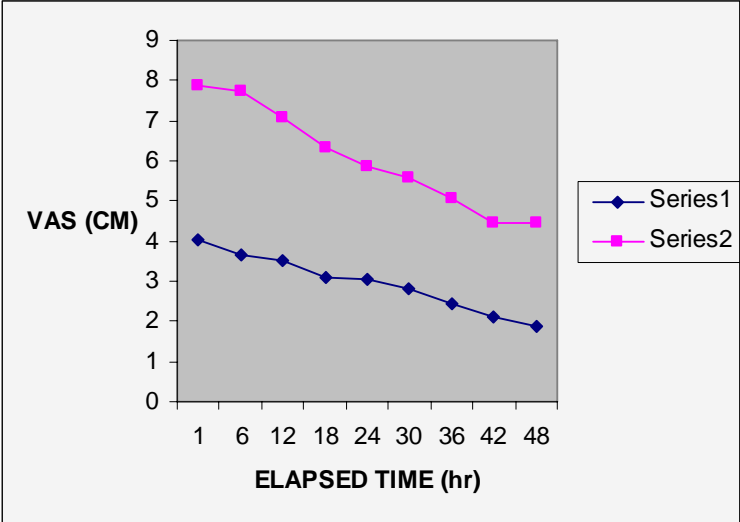
There was significant difference between the groups when comparing mean pain scores ($P < 0.001$). When VAS scores were analyzed at each time point recorded showed significant difference between the groups at any time of measurement (Table 3.)

Table 3 Pain scores

Time	Interpleural Pain score	Control Pain score	P Value
1 Hour	4.0± 1.2	7.8 ± 0.7	< 0.001
6 Hour	3.6 ± 0.8	7.7 ± 0.7	< 0.001
12 Hour	3.5 ±1.0	7.0 ± 1.0	< 0.001
18 Hour	3.1 ± 1.3	6.3 ± 1.0	< 0.001
24 Hour	3.0 ± 1.4	5.8 ± 1.3	< 0.001
30 Hour	2.8 ± 1.4	5.5 ± 1.2	< 0.001
36 Hour	2.4 ± 1.1	5.0 ± 1.2	< 0.001
42 Hour	2.1± 1.2	4.4 ± 1.2	< 0.001
48 Hour	1.8 ± 1.1	4.4 ± 1.1	< 0.001
Total(48 hrs)	2.96 ± 0.72	6.04 ± 1.30	< 0.001

Visual analogue scale (VAS) pain score versus time in patients assigned to pleural bupivacaine (◆) or control group (■). Data are presented as mean ± SD.

Picture



Discussion

The aim of postoperative pain management is to provide good subjective comfort and to contribute to early recovery and a good outcome after surgery.

In this prospective study we have investigated the efficacy of intermittent boluses of interpleural bupivacaine compared to intramuscular pentazocine with regard to postoperative pain relief. Many clinicians avoid the closed chest technique for the placement of an interpleural catheter because of the high incidence of pneumothorax (3). Using our technique, pneumothorax was not seen in our patients as determined by chest x-ray in the recovery room. We used a syringe filled with saline and a Touhy needle instead of a lubricated glass syringe to locate the interpleural space. This may eliminate false negatives caused by sticking between the piston and the syringe wall and thus prevent the needle from being accidentally advanced too far into the thoracic cavity. Our technique is equally effective as the balloon method and it was easy to identify the pleural space.

We used pentazocine for comparison with interpleural bupivacaine because it has less propensity for causing spasm of sphincter of Oddi .

The intramuscular route was chosen because of the simplicity of administration by nurses in the post operative ward.

Nevertheless, the use of interpleural local anesthetics is not devoid of side effects that include pneumothorax (most common), systemic toxicity of local anesthetics, pleural effusion, Horner's syndrome, pleural infections, catheter rupture, and temporary phrenic nerve palsy (16,17).

No such complications were recorded in our patients. Pneumothorax and phrenic nerve palsy were excluded in our patients by chest X-rays.

Furthermore, the use of a diluted local anesthetic solution decreased the propensity for phrenic nerve palsy and toxic reactions.

Parenteral opioids are similarly associated with risks, especially ventilatory depression and cognitive impairment that may restrict early postoperative ambulation. There is significant opioid sparing benefit by the interpleural analgesia.

We have chosen 40 ml of 0.25% bupivacaine every 6 hrs because this dose is unlikely to be associated with toxic plasma concentration.(18)

In fact, postoperative alpha 1-acid-glycoprotein increases, leading to

an increase in protein binding of local anesthetics and to a reduction of free-fraction, thus diminishing the risk of potential central nervous system toxicity (19). Moreover, Scott (20) suggests that the absolute toxic plasma concentration may be more dependent on the rate of increase of the concentration than on any exact concentration of bupivacaine.

Von Kleef et al also found no difference between the use of 0.5% and 0.25% bupivacaine for interpleural analgesia (21). We used 0.25% bupivacaine which produced effective analgesia.

The quality of analgesia obtained in our study is consistent with that reported by others.(2,3,4).

The results of this study demonstrate the effective analgesia obtained in the immediate postoperative period by the injection of interpleural bupivacaine after upper abdominal surgery.

CONCLUSION

It is concluded from this study that intermittent interpleural analgesia with bupivacaine was more effective than intermittent parenteral administration of pentazocine alone , in reducing the severity of pain after upper abdominal surgery up to 48 hours postoperatively and can be recommended for sufficient pain control.

References

1. Kvalheim L, Reiestad F. Intrapleural catheter in the management of postoperative pain. *Anesthesiology* 1984;61: A231.
2. Reiestad F, Stromskag KE. Interpleural catheter in the management of postoperative pain - a preliminary report. *Regional Anesthesia* 1986; 11: 88-91.
3. Brismar B, Petterson N, Tokics L, Strandberg A, Hedenstierna G. Postoperative analgesia with intrapleural administration of bupivacaine-adrenaline. *Acta Anaesthesiol Scand* 1987; 31: 515-20.
4. Stromskag KE, Reiestad F, Holmqvist E, Ogenstad S. Intrapleural administration of 0.25%, 0.37%, 0.5% bupivacaine with epinephrine after cholecystectomy. *Anesth Analg* 1988; 67: 430-4.
5. Rocco A, Reiestad F, Gudman J, McKay W. Intrapleural administration of local anesthetics for pain relief in patients with multiple rib fractures. *Regional Anesthesia* 1987; 12:10-4.
6. Reiestad F, Kvalheim L, McIlvaine WB. Interpleural catheter in the management of acute thoracic herpes zoster. *Regional Anesthesia* (In press)

7. Sihota MK, Ikuta PT, Holmblad BR, Reiestad F, Zsigmond EK.
Successful pain management of chronic pancreatitis and post herpetic neuralgia with intrapleural technique. *Regional Anesthesia* 1988; 13:2S:40.
8. Duranni Z, Winnie AP, Ikuta P. Interpleural catheter analgesia for pancreatic pain. *Anesth Analg* 1988; 67: 479-81.
9. Murphy DF. Interpleural analgesia. *Br J Anaesth* 1993;71:426–34.
10. Frank ED, McKay W, Rocco A, Gallo JP. Interpleural bupivacaine for postoperative analgesia following cholecystectomy: a randomized prospective study. *Reg Anesth.* 1990 ;15(1):26-30.
11. Luc Frenette, Daniel Boudreault, Joanne Guay .Interpleural analgesia improves pulmonary function after cholecystectomy. *Can J Anaesth* 1991 ; 38(1):71-4
12. Schulte-Steinberg H, Weninger E, Jokisch D. Intraperitoneal versus interpleural morphine or bupivacaine for pain after laparoscopic cholecystectomy. *Anesthesiology.* 1995 ;82(3):634-40.
13. Wei-Zen Sun, Yi Chang,, Yung-Tai Chung. Left recurrent laryngeal nerve paralysis after interpleural analgesia. *Anesthesiology* 2003;99:1033-34
14. Brismar B, Pettersson N, Tokics L, Strandberg A, Hedenstierna G.

Postoperative analgesia with intrapleural administration of bupivacaine-adrenaline. *Acta Anesthesiol Scand* 1987; 31: 515-20.

15. Seltzer J Let al. Intrapleural bupivacaine - a kinetic and dynamic evaluation. *Anesthesiology* 1987; 67: 811-3.

16 . Stromskag KE, Minor B, Steen PA. Side effects and complications related to interpleural analgesia: an update. *Acta Anaesthesiol Scand* 1990;34:473-7.

17. A Lauder GR. Interpleural analgesia and phrenic nerve paralysis. *Anaesthesia* 1993;48:315-6.

18.MurphyDF.Interpleural analgesia (see comments).*Br J Anaesth*1993;71;426-34.

19. Wulf H, Winckler K, Maier C, Heinzow B. Pharmacokinetics and protein binding of bupivacaine in postoperative epidural analgesia. *Acta Anaesthesiol Stand* 1988;32:530-4.

20. Scott DB. Toxic effects of local anaesthetic agents on the central nervous system. *Br J Anaesth* 1986;58:732-5.

21. VanKleef JW, Logerman EA, Burm AG et al.Continuous interpleural infusion of bupivacaine for postoperative analgesia after surgery with

flank incisions: a double – blind comparison of 0.25% and 0.5% solutions. *Anaesth Analg* 1992 ;75:268-74.

Pleural analgesia– PROFORMA

DEPARTMENT OF Anaesthesiology
GOVERNMENT GENERAL HOSPITAL, CHENNAI-01.

Sl.No:

Date :

I.P.NO

NAME:	AGE:
SEX:	
Diagnosis:	D.O.O:
Surgery :	
ASA PS : 1 2 yes/No	Allergy to study drugs:
WEIGHT:	Consent

Methods : General anaesthesia with IPPV

Premedication :

Inj Glycopyrrolate 0.2 mg IV

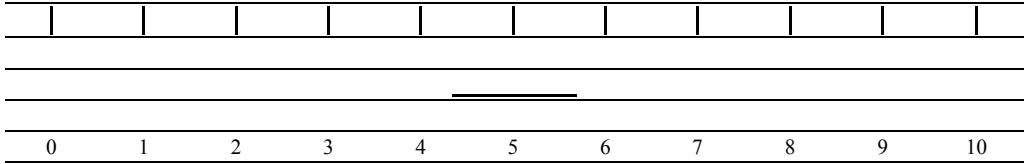
Inj Fentanyl 100 mic IV

Induction : Injpropofol

Inj Succinyl choline

Intubation:

Numerical Scale



No pain _____ Worst pain imaginable

Visual Analog Scale







No pain _____ Worst pain

Directions: Ask the patient to indicate on the line where the pain is in relation to the two extremes. Qualification is only approximate; for example, a midpoint mark would indicate that the pain is approximately half of the worst possible pain.

Categorical Scale

None (0) Mild (1-3) Moderate (4-6) Severe (7-10)

Pain Faces Scale

					
0	2	4	6	8	10
Very happy, no hurt	Hurts just a little bit	Hurts a little more	Hurts even more	Hurts a whole lot	Hurts as much as you can imagine (don't have to be crying to feel this much pain)

Time of catheter removal

Remarks.

MASTER CHART – PLEURAL GROUP

SNO	NAME	AGE(yr)	SEX	POD1(mg)	POD(2)	VAS:1HR	6HR	12HR	18HR	24HR	30HR	36HR	42HR	48HR	SIDE	surgery	Weight(kg)
1	Selvam	36	M	30	30	5	5	5	5	5	4	4	4	2	0	Neph	55
2	parvathy	46	F	60	30	3	3	4	4	4	4	1	1	1	0	Py.plas	45
3	amaravathy	29	F	30	0	5	4	3	3	3	2	2	2	1	0	Py.plas	52
4	raji	28	F	60	30	4	3	4	3	3	3	2	2	2	0	Py.plas	45
5	valliammal	52	F	30	30	2	3	2	2	2	2	2	1	1	0	Neph	56
6	sornam	56	F	30	30	4	4	4	5	4	4	3	3	3	0	Neph	60
7	govindamal	45	F	30	30	4	3	3	2	2	1	1	1	1	0	Py.Lith	70
8	morkayee	46	F	30	30	4	4	4	3	2	2	4	3	3	0	Neph	55
9	amirtham	56	F	30	30	5	4	4	4	3	2	2	1	1	0	Neph	59
10	varalakshmi	36	F	30	30	4	3	3	1	1	1	2	1	1	0	Py.plas	52
11	vellathai	50	F	30	30	4	4	2	2	2	2	2	1	1	0	Chole	60
12	sampath	40	M	30	30	5	4	4	4	5	5	3	3	3	0	Chole	55
13	chinnaponnu	38	F	30	30	3	3	5	4	4	4	4	3	3	0	Chole	60
14	ramamorthy	47	M	30	30	4	5	4	4	3	3	2	2	2	0	Py.Lith	55
15	selvakumar	27	M	30	30	3	3	3	1	1	1	1	1	1	0	Py.plas	55
16	saraswathy	21	F	30	30	2	2	1	1	1	1	1	1	1	0	Py.plas	48
17	baskaran	25	M	30	30	5	5	4	4	5	5	5	5	5	0	Chole	60
18	vijyakumari	55	M	30	30	7	4	4	4	5	5	3	3	2	0	Chole	56

MASTER CHART – CONTROL GROUP

SNO	NAME	AGE(yr)	SEX	POD1(mg)	POD2(mg)	VAS:1HR	6HR	12HR	18HR	24HR	30HR	36HR	42HR	48HR	SIDE	surgery	Weight(kg)
1	pitchai	65	M	90	60	9	8	8	7	7	7	7	6	5	0	Py.plas	50
2	chandraiya	45	M	90	90	9	8	8	7	7	7	6	6	6	0	Neph	60
3	arumugham	46	M	90	60	8	8	7	7	7	7	6	6	5	0	Py.Lith	55
4	paramasivam	46	M	60	60	7	6	5	4	4	2	2	2	2	0	Py.Lith	60
5	nisi	18	F	90	90	9	9	8	5	8	5	5	2	4	0	Py.Lith	50
6	thirupal	46	F	60	60	8	8	6	6	5	5	4	4	3	0	Py.Lith	55
7	rajamani	50	F	60	30	7	7	6	6	5	5	4	4	4	0	Py.plas	50
8	banumathi	35	F	60	30	9	8	9	7	5	5	4	4	4	0	Py.Lith	50
9	ramakrishnan	37	M	60	30	8	7	7	6	8	6	5	5	5	0	Py.Lith	52
10	venkatesh	38	M	60	30	8	8	7	7	6	6	6	5	5	0	Py.plas	75
11	kalaiselvi	48	F	60	30	8	8	7	7	6	6	5	5	5	0	Chole	60
12	malini	46	F	60	30	7	8	8	7	6	6	6	4	4	0	Chole	65
13	hamsaveni	48	F	60	30	7	7	6	6	4	5	5	4	4	0	Chole	60
14	sekar	45	M	90	60	7	7	6	5	5	5	5	4	4	0	Py.Lith	55
15	lakshmanan	62	M	60	30	7	8	8	7	5	5	4	4	4	0	Neph	60
16	babu	40	M	60	30	8	8	7	7	7	7	6	6	7	0	Py.plas	52
17	kamsan	60	M	60	60	8	7	6	5	4	4	4	3	3	0	Py.Lith	66
18	kalaiselvi	22	F	60	30	8	9	8	8	7	7	7	6	6	0	Py.Lith	52

