COMPARING THE OUTCOME OF INTRA-ARTICULAR ANALGESIC BETWEEN BUPIVACAINE AND CHIROCAINE FOR POST ARTHROSCOPY OF THE KNEE

BY

RAEROSS ANAK JABUL

A dissertation submitted in fulfillment of the requirement for the degree of Master of Orthopaedic Surgery

Kulliyyah of Medicine
International Islamic University Malaysia

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ABSTRACT

This prospective and double blinded study to compare effectiveness between Bupivacaine and Chirocaine for intra-articular local analgesia. Bupivacaine involve 28 patients and Chirocaine involve 32 patients who underwent knee arthroscopy of knee in Hospital Tengku Ampuan Afzan. Visual Scale Analog for pain measured 30 minutes, 6 hours, 8 hours and 24 hour post knee arthroscopy. All 60 patients involve in this study. In total 28 patients randomized for Bupivacaine post arthroscopy and 32 patients randomized for Chirocaine. The total patient bases on gender were 44 involved male patients and 16 involves females patient with ratio 4 to 1. The assessment pain score post-arthroscopy of all patients within 24 hour with Visual Analogue Scale (VAS).Patient discharged after 24 hour post-procedures. In conclusion, Bupivacaine is an effective analgesic and superior compare Chirocaine.

APPROVAL PAGE

I certify that I have supervised and read this study and that in my opinion, it conforms to acceptable standards of scholarly presentation and is fully adequate, in scope and quality, as a dissertation for the degree of Master of Orthopaedic Surgery

…….
Aminudin Che Ahmad
Supervisor

…….
Mohamed Azril Mohamed Amin
Co-Supervisor

…….
Rozilah @ Abdul Hadi Bin Mohamed
Co -Supervisor

This dissertation was submitted to the Department of Orthopaedic and is accepted as a fulfillment of the requirements for the degree of Master of Orthopaedic Surgery

……...
Mohamed Azril Mohamed Amin
Head, Department of Orthopaedics, Traumatology and Rehabilitation

This dissertation was submitted to the Kulliyyah of Medicine and is accepted as a fulfillment of the requirements for the degree of Master of Orthopaedic Surgery

……
Azmi Md Nor
Dean, Kulliyyah of Medicine

DECLARATION

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Raeross Anak Jabul

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VAS	Visual Analog Score

CHAPTER ONE

INTRODUCTION

1.1 INTRODUCTION

Knee arthroscopy is a common procedure in orthopaedic department. This is usually considered as a minimal invasive surgery. Arthroscopy can be performed as a day care procedure or discharge on the next day post-surgery procedure. Patient usually underwent procedures such as a diagnostic arthroscopy, meniscus debridement and tendon repair.

Patient most commonly sustained meniscus with anterior cruciate ligament injury and needed repair and debridement. Occasionally patient also needed diagnostic arthroscopy to confirm the injury if Magnetic Resonance Imaging is in doubt. Post-arthroscopic there was reported a significant number of patients have moderate to severe pain within 24 hours post-surgery. Spinal anaesthesia is widely used for knee arthroscopy procedures because of its fast onset and longer duration of anaesthesia however, it is also associated with an incidence of transient neurological symptoms.

The employment of local anaesthesia in knee arthroscopy is a common technique. Local anaesthesia often used for the management of pain after arthroscopic knee surgery. A long acting local anaesthesia is a choice such as Bupivacaine. The advancement of arthroscopic surgery and sport medicine over the last decades especially in Malaysia regarding the treatment through arthroscopic in view of diagnostic and treatment with minimal invasive technique. This increases the numbers of arthroscopic procedure either as in patient or as a day care procedure.

Post diagnostic arthroscopic and debridement analgesic is one of the most important aspects of post care surgery. Many method of post- operative pain management employ for the comfort of patient. Zeng et al and Wei et al evaluated and meta-analysed postoperative pain intensity subsequent to intra-articular analgesia with Bupivacaine and morphine results from the meta-analyses on pain showed significant improvements in pain score and additional analgesia. In his review article, Baillieul et al, stated that Bupivacaine is equally potent compare to Levobupivacaine for post arthroscopic pain management (RJ Bailieul, 2009). A single intra articular injection of Bupivacaine is a common practice and safe for post arthroscopy surgery (Webb and Ghosh, 2009). A practice of continues Bupivacaine with pump infusion post anterior cruciate ligament reconstruction for 48 hours showed decreased and reduce in narcotic consumption (Heizn , 2009).

Most studies shows differences in results, in term of outcome for intra-articular analgesia in term of post-arthroscopy pain management. The study of single intra-articular injection with Bupivacaine as a local anaesthesia because of it safety and long duration of action but there is no local study comparing with Levobupivacaine. A review of 20 studies by P. N Convery et Al, showed there was no adverse effect or toxicity post intra-articular local anaesthesia administration for knee surgery (Gustafsson, Convery, Milligan, Quinn, & Sjo, 2001). Study by Rao et al, concluded combination of Bupivacaine and ketorolac effective intra-articular analgesia following knee arthroscopy (Rao, Orth & Orth, 2005). There was study in Turkey, showed there was no difference post pain score between Bupivacaine and Levobupivacaine (Karaman, Kayali, Ozturk, Kaya, & Bor, n.d., 2007).Intra-articular Bupivacaine is an effective analgesic in management of pain following arthroscopic knee surgery (Reuben & Sklar, 2000.).

The main purpose of this study is to find a simple method, safe and cost effective for post knee arthroscopy surgery. The analgesia is a choice because both is a long acting analgesia and a safe local anaesthesia. In view of Levobupivacaine has a long duration of action compare to Bupivacaine, compare the outcome of long acting analgesic between Bupivacaine and Levobupivacaine. Hopefully this study will establish the consensus use of intra-articular local anaesthesia for post arthroscopy knee surgery pain management. This study was conducted among patient who underwent diagnostic arthroscopic and debridement in Hospital Tengku Ampuan Afzan.

1.2 OBJECTIVES AND HYPOTHESIS

1.2.1 General Objective

- To determine the efficacy of intra-articular analgesia post-arthroscopic diagnostic and debridement.
- To evaluate whether intra-articular local anesthesia Chirocaine and Bupivacaine adequate to control pain within first 24 hours post knee arthroscopy patients.
- To study and evaluate a better pain management and patient satisfaction

1.2.2 Specific Objectives

1. To assess pain score post-arthroscopy of all patient within 24 hour with Visual Analogue Scale (VAS) by comparing Bupivacaine in comparison to Chirocaine.
2. To evaluate the pain in static (0 degree) and in flexion movement (60 degree)
3. To measured additional analgesia needed post-arthroscopic debridement.

4. To provide evidence based recommendation for use of local analgesic for knee arthroscopy procedures

1.2.3 Hypothesis

There is no significant improvement postoperative pain score with visual analogue score and additional analgesic post knee arthroscopic procedure comparing Bupivacaine and Chirocaine.

CHAPTER TWO

LITERATURE REVIEW

2.1 ANATOMY OF KNEE.

Knee joint is a synovial joint and largest in the body. It is a modified hinge joint with a flexion and extension movement. It is consist of two condylar joints between the femur, tibia and patella. Both the left and right femurs converge toward the knee and each tibia is nearly vertical, femur and tibia meet at an angle of between 5-12 degrees. The surface of medial condyle is larger, more curved and projects further than lateral condyle, accounting for the angle between femur and tibia. The lateral tibia articular surface is almost circular and the medal side is oval with a longer antero-posterior axis. The articular surface of the patella is divided by a vertical ridge into a large lateral and a small medial surface. The large lateral area articulates with the lateral condyle of the femur in extension and flexion.

The capsule of the knee joint is attached posteriorly to the proximal margin of the femoral condyles and the intercondylar fossa. Medially is attached to the margin of the femur but laterally is attached proximal to the groove for the popliteus tendon. Anteriorly the capsular attachment on the femur is deficient above the level of the patella. This allowed the suprapatellar bursa to be in contact with the joint. The capsule is gaining attachment to the side of the patella and patellar ligament. The capsule is attached posteriorly on the tibia condyle margin and in the intercondylar area to the edge of the groove for the posterior cruciate ligament. The attachment to the lateral condyle is interrupted by an aperture for the passage of the popliteus. On the lateral side, the capsule is attached to the margin of the tibial condyle and laterally

to the head of the fibula. A thicken capsule on the medial side is a deep component of the tibial collateral ligament and firmly attached to the medial meniscus. The deep aspect it has weak attachment to the rims of both meniscus and coronary ligament attached them to the tibia. Anteriorly the attachment to the tibia of the fused capsule and patellar retinacula inclines distally from the medial and lateral condyle to the tibial tuberosity.

The blood supply of the knee joint is mainly from the anastomoses around the knee. There are five genicular artery branches of the popliteal. The knee joint nerve supply is from the femoral nerve through its branches to the three vasti, the sciatic nerve through the genicular branches of its tibial and common peroneal nerve components and from the obturator nerve along femoral artery through the gap in the adductor magnus into the popliteal fossa.

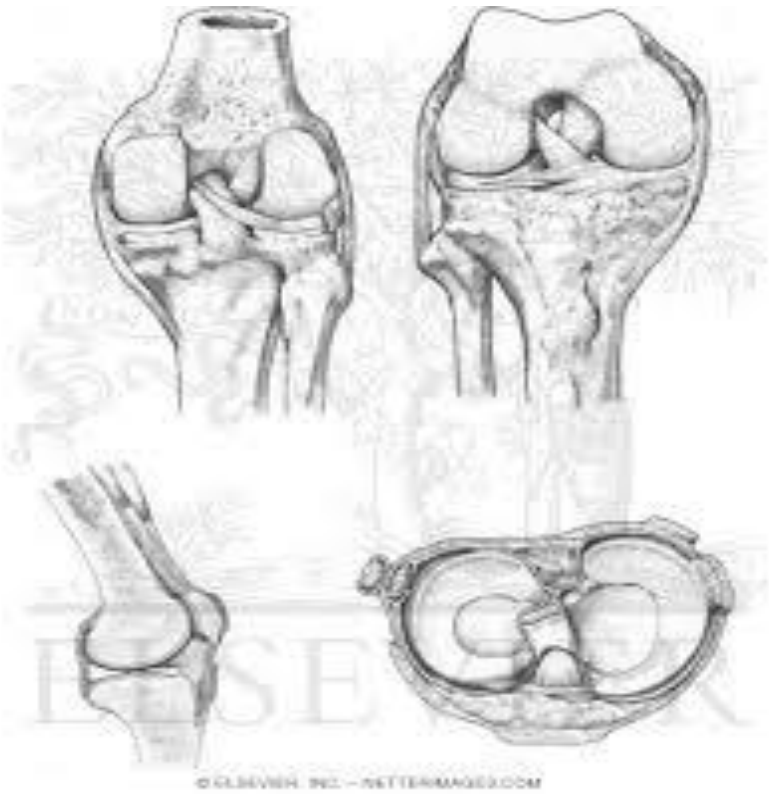

Figure 1.1 Anatomy of the knee.

2.2 KNEE ARTHROSCOPY.

Orthopaedic surgeons perform arthroscopic surgery in many joints of the extremities, most commonly the knee. The benefit of arthroscopy in diagnosis, debridement in non- degenerative disease and meniscal repair cannot be denied. As technologies progress, orthopaedic surgeons are able to perform more complex procedures using arthroscopic equipment such ACL repair. A combination of pre and post anterior cruciate ligament reconstruction with intra-articular injection of Bupivacaine reduces analgesic consumption significantly (Butterfield et al., 2000). Diagnostic arthroscopy procedure of knee, enable a surgeon to visualize if the pathology not visible on a radiograph for surgeon to diagnose and to perform operative procedure at the same setting. This procedure is a minimal invasive technique and advocates the procedure to perform as a day care procedure.

Around a quarter of people, aged 55 years or more in the United Kingdom has persistent pain (Bruce Et Al., 2004). Around 700,000 arthroscopic partial meniscectomies were performed annually in the United States annually with estimated cost of $4 billion (Sihvonen et al., 2013). Osteoarthritis is the single most common cause of disability in older adults, with 10% of patients aged 55 or more having painful disabling osteoarthritis of the knee, a quarter of whom are severely disabled. Patients with osteoarthritis, over 80% will have limitation of movement and greater than 25% unable to perform their activities of daily living (Li et al., 2008). Arthroscopy for knee osteoarthritis has remained a topic of controversy amongst clinicians. Multiple clinical trials discuss the efficacy of arthroscopic debridement in the treatment of knee osteoarthritis. The procedure serves to remove the products of cartilage wear, mechanical irritations, inflammatory cells and molecules from the joint; therefore counter the onset of painful inflammatory phases of osteoarthritis.

However, osteoarthritis is not a contraindication to arthroscopic surgery, and arthroscopic surgery remains appropriate in patients with arthritis in specific situations in which osteoarthritis is not believed to be the primary cause of pain. Even a recent trend shows there are no benefit in arthroscopic surgery in a OA patient the benefit in term of diagnostic and meniscal repair more beneficial to patient.

A randomized placebo-controlled trial study conducted in Norway showed only 76 % developed moderate to severe pain after 1 hour post knee arthroscopic procedure (Breivik, 2004). There were study done in the past compared morphine and Bupivacaine with an inconsistent results. The main factors influence the result are the dose administered, volume of the medication, variable use of tourniquets, degree of manipulation with debridement, surgeon experience and perioperative pain. The application of tourniquet also reduce systemic absorption of Bupivacaine increase it safety and effectiveness (S T Chan, 1995). Pain score one hour post knee arthroscopy directly related with an increase of tourniquet time and perioperative pain score (Gustafsson et al., 2001). Follak and Ganzer, performed a prospective randomized, double-blind study comparing use of Bupivacaine with morphine for several surgical procedures, including notchplasty, bone-patellar tendon-bone autograft, anterior cruciate ligament reconstruction, and meniscectomy found that Bupivacaine was more effective than morphine for postoperative pain control (Follak and Ganzer, 2001). De Andres et al., compared use of morphine to Bupivacaine and a combination of both showed no difference existed among the groups for postoperative pain control (De Andres J, Valia JC, Barrera L and Colomina, 1998). McSwiney et al., performed study comparing use of a placebo, morphine, Bupivacaine, and morphine with Bupivacaine. They found that the combination of morphine and Bupivacaine was the most effective in reducing postoperative pain scores McSwiney MM, Joshi GP, Kenny P and

McCarroll SM, 1993). S T Chan in his study found, morphine significantly reduce pain until 4 hours post intra-articular injection and Bupivacaine beyond 4 hours duration but no significant after 24 hours (S T Chan 1995). Intra-articular morphine is as effective as Bupivacaine for postoperative pain control for partial meniscectomy and chondral debridement of the knee (E, K, Ms, & C, 2013). This will reduce patient time warded in the hospital, allowing a quicker and easier recovery with saving on analgesic cost for pain killer. Beside knee arthroscopy surgery, second most common intra-articular local anaesthesia injection is shoulder arthroscopic procedure. Shoulder arthroscopic rotator cuff repair with continues pump infusion of Bupivacaine showed significant reduce in VAS pain score and narcotic consumption (Fronek & Hoenecke, 2008).

The purpose of this study is to compare Bupivacaine as gold standard with Levobupivacaine for single intra-articular local anaesthesia injection. This will provide a better post-arthroscopic pain management for the patient. This also can reduce the side effect of opioid analgesic and non-steroid anti-inflammatory drug reaction and option for patient with allergic to opioid and NSAID analgesic.

2.3 LOCAL ANAESTHESIA.

The option of local anaesthesia for post arthroscopic procedures is a long acting local anaesthesia. Many studies performed long acting local anaesthesia as a choice because the benefit in term of onset and duration of action.

Local anaesthetics block the generation and the conduction of nerve impulses, by increasing the threshold for electrical excitation in the nerve, slowing the propagation of the nerve impulse, and reducing the rate of rise of the action potential. In general, the progression of anaesthesia is related to the diameter, myelination, and

conduction velocity of affected nerve fibres. Clinically, the order of loss of nerve function is as follows: pain, temperature, touch, proprioception, and skeletal muscle tone. Systemic absorption of local anaesthetics produces effects on the cardiovascular and central nervous systems (CNS). At blood concentrations achieved normal therapeutic doses, changes in cardiac conduction, excitability, refractoriness, contractility, and peripheral vascular resistance are minimal. However, toxic blood concentrations depress cardiac conduction and excitability, which may lead to atrioventricular block, ventricular arrhythmias, and cardiac arrest, sometimes resulting in fatalities. In addition, myocardial contractility is depressed and peripheral vasodilation occurs, leading to decreased cardiac output and arterial blood pressure. Local anaesthetics can produce central nervous system stimulation, depression, or both. Apparent central stimulation is manifested as restlessness, tremors and shivering progressing to convulsions, followed by depression and coma progressing ultimately to respiratory arrest. Depending upon the route of administration, local anaesthetics are distributed to some extent to all body tissues, with high concentrations found in highly perfused organs such as the liver, lungs, heart, and brain. In clinical studies, elderly patients reached the maximal spread of analgesia and maximal motor blockade more rapidly than younger patients. Elderly patients also exhibited higher peak plasma concentrations following administration of local anaesthesia. The total plasma clearance was decreased in these patients. Metabolized primarily in the liver via conjugation with glucuronic acid. Patients with hepatic disease, especially those with severe hepatic disease, may be more susceptible to the potential toxicities of the amide-type local anaesthetics. The kidney is the main excretory organ for most local anaesthetics and their metabolites. Urinary excretion is affected by urinary perfusion

and factors affecting urinary pH. Only 6% of Bupivacaine is excreted unchanged in the urine.

Bupivacaine is amino amide group with 2-Piperidinecarboxamide, 1-butyl-N-(2, 6dimethylphenyl)-, monohydrochloride, monohydrate, a white crystalline powder that is freely soluble in 95 percent ethanol, soluble in water, and slightly soluble in chloroform or acetone. Bupivacaine is available in sterile isotonic solutions for injection via local infiltration, peripheral nerve block, and caudal and lumbar epidural blocks. Solutions of Bupivacaine may be autoclaved and the solutions are clear and colourless. Bupivacaine is related chemically and pharmacologically to the aminoacyl local anaesthetics. It is a homologue of mepivacaine and is chemically related to lidocaine. This anaesthetics contain an amide linkage between the aromatic nucleus and the amino, or piperidine group. They are different in this respect from the procaine-type local anaesthetics, which have an ester linkage. The onset of action with Bupivacaine is rapid and considered as a long acting local anaesthesia. The onset of action following injection is usually 2 to 10 minutes and anaesthesia may last two or three times longer than lidocaine, in many patients up to 7 hours. Bupivacaine with a high protein binding capacity (95%) but has a low fetal/maternal ratio (0.2 to 0.4). The extent of placental transfer is also determined by the degree of ionization and lipid solubility of the drug. Lipid soluble, non-ionized drugs readily enter the fetal blood from the maternal circulation.

Pharmacokinetic studies on the plasma profile of Bupivacaine after direct intravenous injection suggest a three-compartment open model. The first compartment is represented with rapid intravascular distribution of the drug. The second compartment represents the equilibration of the drug throughout the highly perfused organs such as the brain, myocardium, lungs, kidneys, and liver. The third

compartment represents an equilibration of the drug with poorly perfused tissues, such as muscle and fat. Meinig et al, found venous samples of plasma Bupivacaine levels after intra-articular injection of 30 mL of 0.5% Bupivacaine with mean plasma levels less than 650 ng/mL with a peak level at 20 minutes after injection. This unlikely cause toxicity without a direct intravascular administered (Liguori, Figgie, Chimento, & Borow, 2002). The elimination of drug from tissue distribution depends largely upon the ability of binding sites in the circulation to carry it to the liver where it is metabolized. The widely use of Bupivacaine rise the concern of its toxicity and safety to intra-articular surface. Study showed intra-articular Bupivacaine 0.5% lead to articular surface inflammation and synovial changes in rabbit. Toxicity of Bupivacaine is dependent on duration of exposure and dose dependent. In bovine and human articular chondrocyte culture showed 0.5% and 0.25% cause chondrocyte toxicity and 0.125% Bupivacaine and normal saline 0.9% was no different (British Journal Of Anaesthesia, 2009). The adverse effect on joint post intra-articular injection was not established. The post-arthroscopic glenohumeral chondrolysis has been reported but multifactorial such as bio-absorbable implant, severity of the disease and blood supply to the humerus in compare to the knee joint. There are multifactorial has to be considered between experimental studies and clinical such as dilution of Bupivacaine with synovial fluid and absorption to surrounding tissue and arthroscopic fluid lavage. There was no such case reported in post knee arthroscopy procedure with intra-articular local anaesthesia injection.

Levobupivacaine is a local anaesthetic drug belonging to the amino amide group. It is the s-enantiomer of Bupivacaine. Compared to Bupivacaine, Levobupivacaine is associated with less vasodilation and has a longer duration of action. It is approximately 13 percent less potent (molarity) than Bupivacaine and has

a longer motor block onset time. Levobupivacaine, is a better local anaesthesia in term of safety and duration of action. Clinically, Levobupivacaine has been observed to be well-tolerated in regional anaesthesia techniques both after bolus administration and continuous post-operative infusion. The incidence of side effect is rare when it is administered safety dose and accurately.

Levobupivacaine ([2S]-1-butyl-N-2 6-dimethylphenyl] piperidine-2-carboxamide) is an amino-amide local anaesthetic drug belonging to the family of n-alkyl substitute Pipecoloxylidide. Its chemical formula is C18 H28 N2 O.

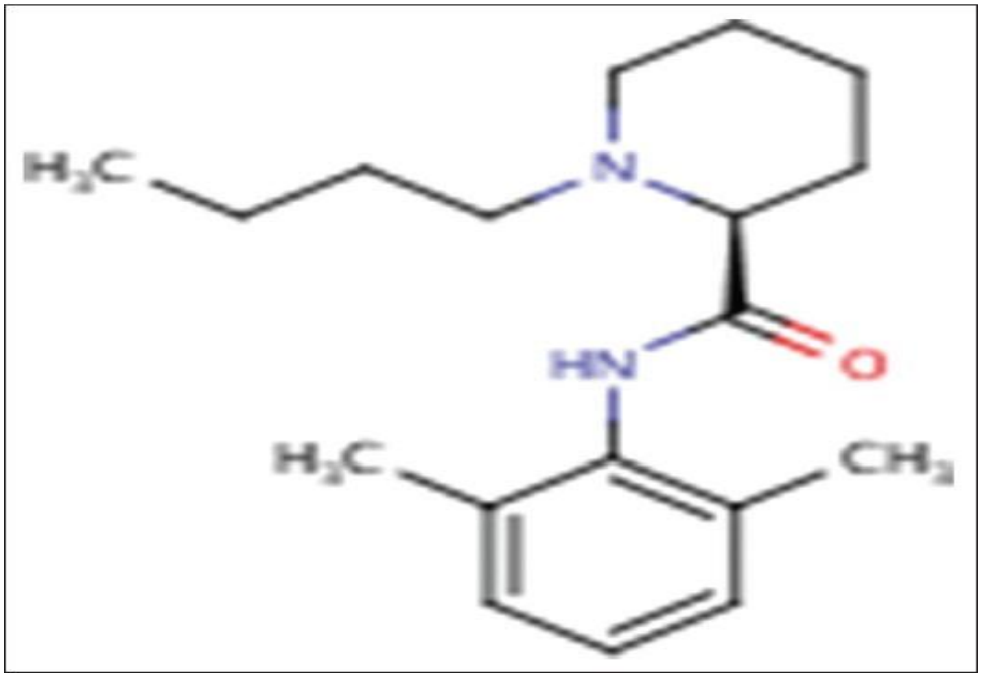

Figure 2.1 Chemical Composition of Levobupivacaine

Levobupivacaine exerts it pharmacological action through reversible blockade of neuronal sodium channels. Myelinated nerves are blocked through exposure at the nodes of Ranvier more readily than unmyelinated nerves. In general, the progression of anaesthesia is related to the diameter, myelination and conduction velocity of the affected nerve fibres. Specifically, the drug binds to the intracellular portion of sodium

channels and blocks sodium influx into nerve cells, which prevents depolarization. It blocks nerve conduction in sensory and motor nerves mainly by interacting with voltage sensitive sodium channels on the cell membrane. The dose as well as the route of administration of Levobupivacaine determines the plasma concentration following therapeutic administration as the absorption is dependent upon the vascularity of the tissue. The volume of distribution is estimated at 66.91 ± 18.23 L. The pKa of Levobupivacaine is 8.1, similar to the pKa of the Bupivacaine. The half-life is 3.3h. The rate of clearance is 39.06 ± 13.29 L/h (after intravenous administration of 40 mg). Alpha1-glycoprotein is the main binding site for Levobupivacaine. Protein binding of Levobupivacaine is more (97%) than Bupivacaine (95%). Less than 3% of the drug circulates free in plasma. Levobupivacaine is extensively metabolized with no unchanged Levobupivacaine detected in urine or feces. Levobupivacaine has a safety margin of 1.3. The concentration necessary to produce cardiac and neurotoxicity is higher for Levobupivacaine compare to Bupivacaine