A RANDOMISED CONTROL STUDY COMPARING THE EFFICACY OF 0.25% ISOBARIC BUPIVACAINE TO 0.5% HYPERBARIC BUPIVACAINE DURING SPINAL ANESTHESIA FOR HIP SURGERIES IN PEOPLE AGED 60 YEARS AND ABOVE.

A DISSERTATION SUBMITTED IN PART FULFILLMENT OF THE REQUIREMENT

OF THE DR.M G R MEDICAL UNIVERSITY, CHENNAI, FOR M.D

(ANESTHESIOLOGY) APRIL 2014

CERTIFICATE

This is to certify that the work carried out in this thesis entitled **"A RANDOMISED CONTROL STUDY COMPARING THE EFFICACY OF 0.25% ISOBARIC BUPIVACAINE TO 0.5% HYPERBARIC BUPIVACAINE DURING SPINAL ANESTHESIA FOR HIP SURGERIES IN PEOPLE AGED 60 YEARS AND ABOVE"** was carried out by Dr. Juliana Josphine. J in the department of anesthesia, Christian Medical College, Vellore under my supervision and guidance.

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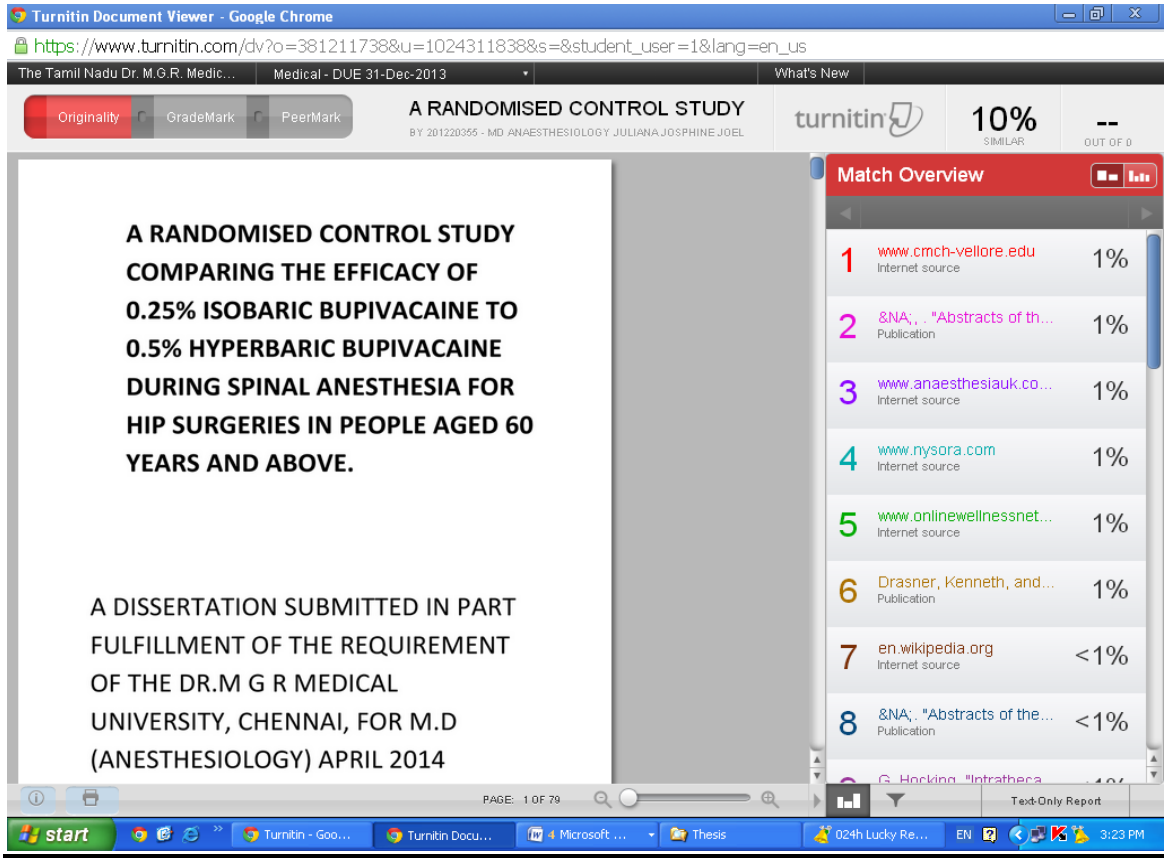
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CONTENTS

Aims and Objectives

Aims and objectives

To compare efficacy of two solutions used for spinal anesthesia, 3ml of 0.5% hyperbaric bupivacaine and 6ml of 0.25% isobaric bupivacaine in the patients aged 60 years and above, posted for hip surgeries in providing stable hemodynamics.

To compare the adequacy and efficacy of these two drugs by looking at the time of onset, height of block, intensity of sensory and motor blockade, duration of anesthesia as well as the incidence of side effects between the two groups were the secondary objectives.

Introduction

Introduction

Spinal anesthesia is one of the most common methods of neuraxial blockade used worldwide, to provide regional anesthesia. It is mainly used for surgeries involving the lower limbs and the abdominal region below the level of the umbilicus.

It involves injecting a drug, usually a local anesthetic agent into the subarachnoid space. The subarachnoid space contains the cerebrospinal fluid (CSF) which bathes the spinal roots and the spinal cord completely.

The major advantage with spinal anesthesia is the ability to control the level of anesthesia and the duration of anesthesia depending on the drug, dosage, concentration and the patient position during and immediately after spinal anesthesia. The most commonly used local anesthetic for spinal anesthesia is hyperbaric bupivacaine of 0.5% concentration, which contains 8% dextrose in order to make it a hyperbaric solution. This drug has stood the test of time and is still being used successfully in most centers throughout the world as it provides good motor and sensory blockade.

Though spinal anesthesia is extremely popular and known for its benefits like decreased mortality and morbidity, early ambulation and discharge from hospital and decrease in the thromboembolic events, it comes with its own set of complications. Some of the most common side effects are hypotension and bradycardia that occur due to the sympathetic blockade. This could be detrimental in the aging population as they are known to have multiple intercurrent illnesses and this increases their morbidity and mortality .(1)

By altering the drug characteristics, we can limit the degree of hemodynamic instability and thereby probably cause a decrease in morbidity and mortality of the patient. The major challenge with spinal anesthesia is to administer enough dose or volume of the local anesthetic agent to provide adequate analgesia and motor blockade during the entire duration of surgery while making sure that there is no chance of high spinal, total spinal or other unwanted side effects. Also the intent of every anesthetist is to provide spinal anesthesia with the least drop in blood pressure and heart rate.

By means of this study, we aspire to show that altering the drug characteristics may limit the degree of hemodynamic instability and at the same time assess if the altered drug characteristics provide adequate motor and sensory blockade.

HISTORY OF SPINAL ANAESTHESIA:

Spinal anesthesia was first described by James Leonard Corning in the year 1885. Later in 1889, Augustus Karl Gustav Bier, a German surgeon used cocaine intrathecally to provide regional anesthesia and perform lower limb surgeries in six patients which included 2 children.(2) He then tried it on his assistant, dr. Otto Hildebrandt and was thrilled to find out that he was insensitive to all sorts of painful stimuli applied to the lower limbs. Though spinal anesthesia became extremely popular in the later part of the 19^{th} century, the interest in the field declined due to the effects and complications of cocaine used intrathecally. It was after the discovery of drugs like lignocaine and bupivacaine that the interest in the field was rekindled. In recent times regional anesthesia has become more popular owing to its benefits over general anesthesia and hyperbaric bupivacaine has become one of the most commonly used intrathecal local anesthetic drug.

The spinal needle has also gone through major modifications in terms of its diameter and design of the tip of the needle overtime due to the some common side effects like post dural puncture headache. The gauge of the needle has increased overtime which implies that the needle is of much smaller diameter now and the needle itself has gone through a dramatic change in terms of its structure and design. The first needle used by Corning was a flexible hollow needle made up of gold or platinum and it had a needle stop and set screw so as to fix the needle at the particular length. It also had a long bevel resulting in increased failure rates and greater loss of CSF. The needle used by Bier to provide surgical anesthesia to his patients was a Quincke's needle. But later he designed a long, large bore needle without an introducer. The disadvantages of large bore needle were soon realized and it paved the way for the development of the Bainbridge needle. It was

the first needle to have stylet with a similar short bevel and a small hub to attach a syringe.

Then came Baker, he designed the first blunt tipped needle but he also used a large bore firm needle. Hoyt was one of the first to introduce the two needle technique, a large introducer and an inner flexible hollow needle. Greene then put forward an atraumatic, beveled end smaller needle made of stainless steel that became very popular. Over the years further developments were made till whitacre and hart introduced their needle which was a pencil tipped closed end needle with a lateral orifice.(3)

Today some of the most commonly used needles for spinal anesthesia in daily practice are divided into two groups depending on the tip of the needle and they are dura separating pencil point and dura cutting sharp edged needles respectively. The incidence of post dural puncture headache and epidural blood patch rates are much less with the pencil tipped dura separating needles along with certain advantages like ease of insertion, ability to perceive the needle crossing different structures due to its blunt tip and low resistance to drug administration.(4)(5) Hence dura separating blunt tipped (Whittacre) needles were used for spinal anesthesia in this study.(6)

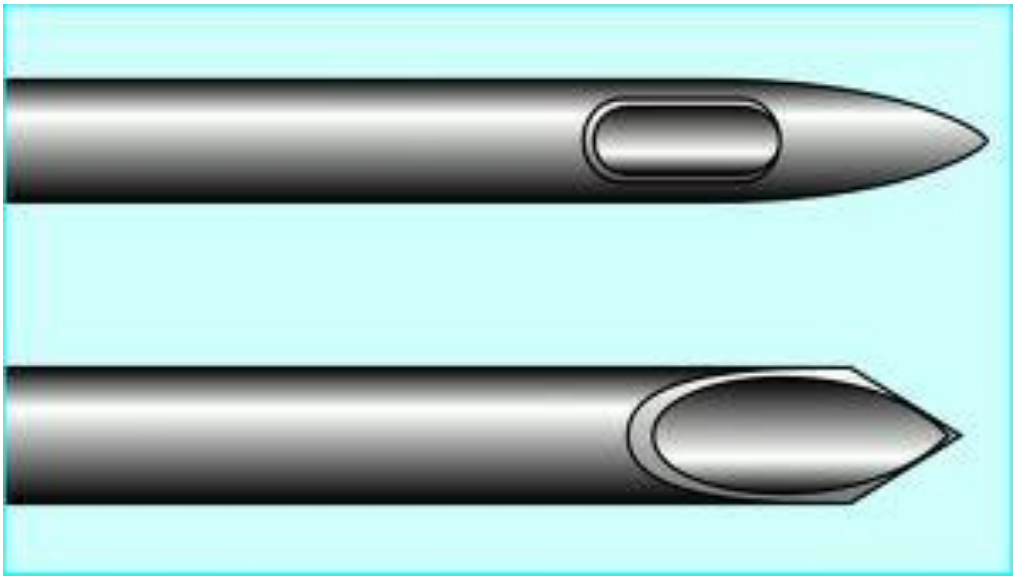


FIGURE 1: PENCIL TIPPED ATRAUMATIC NEEDLE AND SHARP EDGED DURA CUTTING NEEDLE.

Anatomy:

Spinal anesthesia can be successfully used in a number of conditions but in order to conduct a safe procedure, thorough knowledge of the relevant anatomy, pharmacology of local anesthetics, physiological effects of spinal anesthesia, technique and complications is necessary.

Vertebral column:

There are 33 vertebrae in the spinal column of which 7 are cervical, 12 thoracic, 5 lumbar, 5sacral and 4 are coccygeal. The vertebral column has two curvatures that are convex anteriorly, the cervical and lumbar curvatures. The resulting thoracic and sacral curvatures are convex posteriorly. These curvatures of the spine play an important role in determining the extent of spread of the local anesthetic.

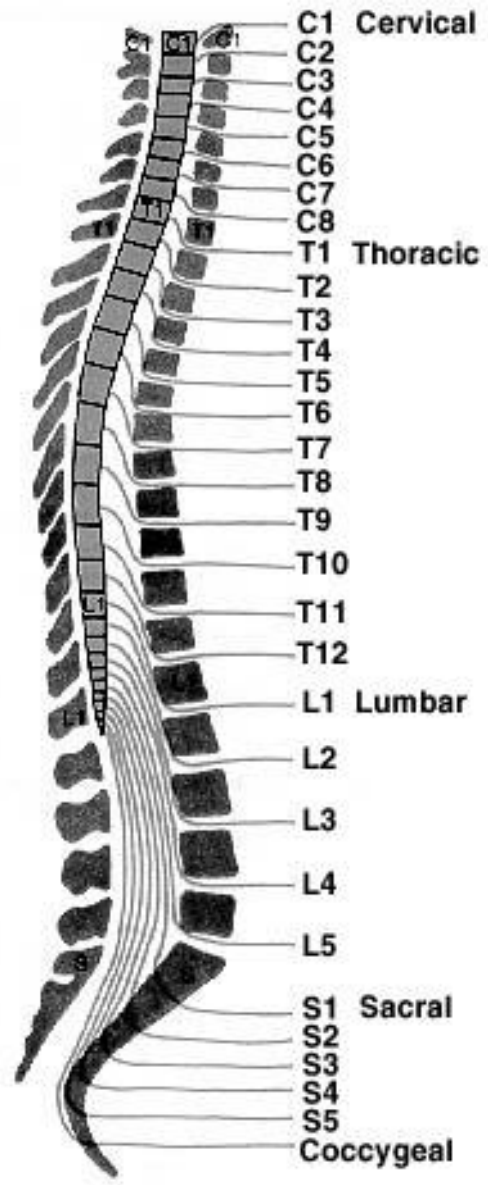


FIGURE 2: VERTEBRAL COLUMN

Spinal ligaments:

There are about five ligaments that hold the spinal column together and they are the supraspinous, interspinous, anterior and posterior spinal ligaments and the ligamentum flavum. Of these the supraspinous ligament connects the apices of the spinous processes from C7 to S2, while the interspinous ligament holds the spinous processes together. The ligamentum flavum binds the laminae above and below, while the anterior and posterior ligaments bind the vertebral bodies together.

Spinal cord:

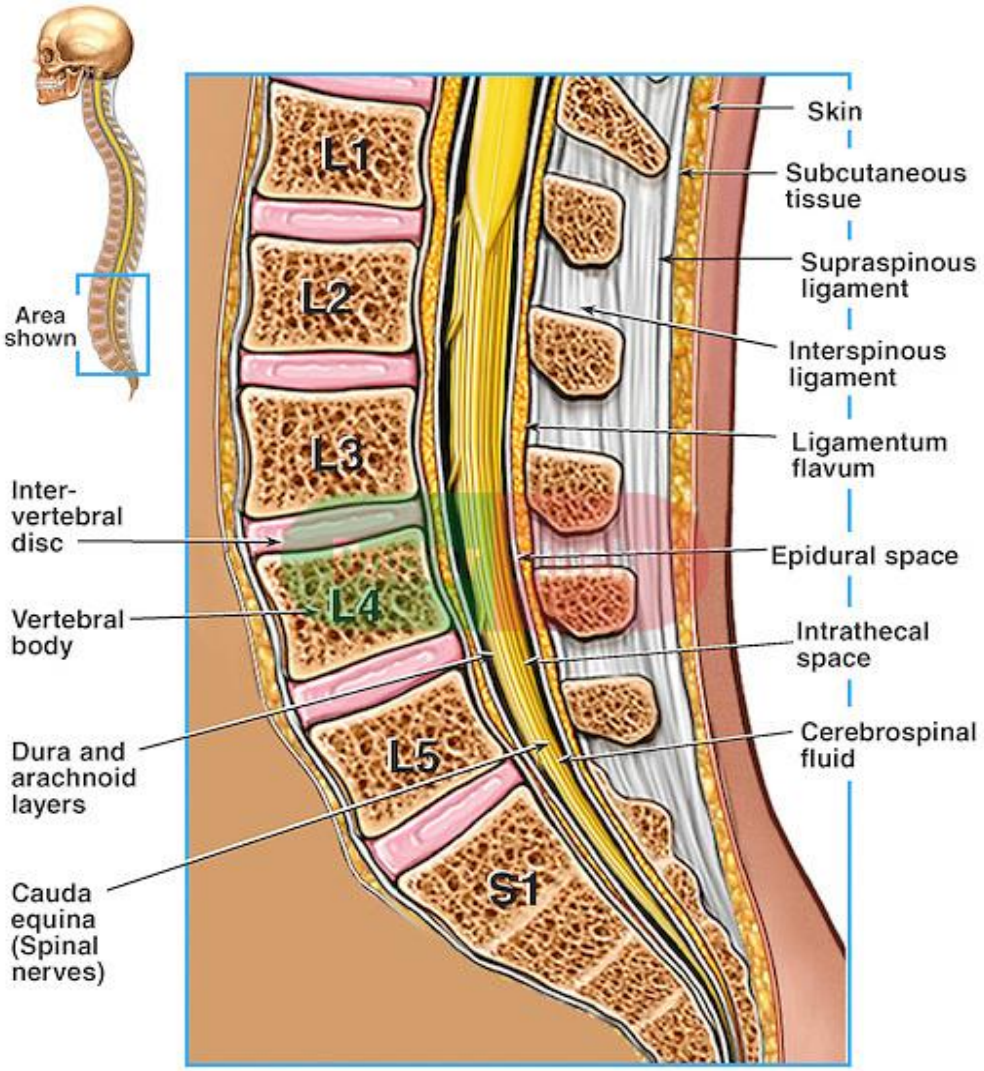
The spinal cord in an adult is about 45cms long and is an elongated cylindrical structure that is flattened anteroposteriorly. The spinal cord begins at the foramen magnum and extends upto the first or second lumbar vertebral space and then forms the conus medullaris below. It extends further as a thin filamentous structure called the filum terminale that gets attached to the coccyx.

The bundles of spinal nerves below the level of the conus medullaris are called the cauda equina.

Spinal meninges:

The spinal is covered by the three meninges: duramater, arachnoid mater and piamater which cover the brain as well. The duramater is the outermost and the toughest of the three layers, while the arachnoid forms a delicate non vascular middle layer that is closely attached to the duramater. The piamater is the innermost layer closely investing the spinal cord and it is a highly vascularised layer.

FIGURE 3: CUT SECTION OF LUMBAR SEGMENT O THE VERTEBRAL COLUMN



There are three compartments that are closely related to the meninges and they are the epidural, subdural and subarachnoid spaces. The epidural space lies outside the dura but within the vertebral canal and it contains the fat, blood vessels, nerve roots and lymphatics which are not distributed uniformly but appear in compartments. The subdural space is the space between the duramater and the arachnoid mater and is a potential space as the arachnoid mater is in close contact with the duramater.

The subarachnoid space contains the cerebrospinal fluid (CSF) and communicates with the tissue spaces around the vessels in the piamater. This is the space we need to encounter in case of spinal anesthesia as the local anesthetic given into this space will combine with the CSF and bathe the spinal nerve roots emerging out of the spinal cord.

The spinal cord usually ends at the lower border of L1 or upper border of L2 in adults but ends at L3 in children. The spinal cord is divided into multiple segments with a pair of spinal nerves arising from each segment. There are about 31 pairs of spinal nerves arising from the spinal cord and these pairs of nerves are symmetrically arranged. Each nerve is formed by the fusion of anterior and posterior nerve roots and immediately distal to this anastamosis the posterior root carries a ganglion. The anterior roots carry the motor fibers while the posterior root carries the sensory fibers.

BLOOD SUPPLY:

The spinal cord is supplied with blood by three arteries that run along its length starting in the brain, and many arteries that approach it through the sides of the spinal column. The three longitudinal arteries are called the anterior spinal artery, and the right and left posterior spinal artery. These travel in the subarachnoid space and send branches into the spinal cord. The anterior spinal artery supplies the entire length of the cord in front of the

posterior grey column and the posterior spinal arteries supply the grey and white columns on either side. The major contribution to the arterial blood supply of the spinal cord below the cervical region comes from the radially arranged posterior and anterior radicular arteries, which run into the spinal cord alongside the dorsal and ventral nerve roots, but with one exception, they do not connect directly with any of the three longitudinal arteries. The largest of the anterior radicular arteries is known as the artery of Adamkiewicz, or anterior radicularis magna (ARM) artery, which is a direct supply from the aorta usually, arises between L1 and L2, but can arise anywhere from T9 to L5. Venous drainage is by the anterior and posterior spinal veins which eventually drain in to the segmental veins that communicate with the medullary veins.

CEREBROSPINAL FLUID:

CSF is formed by the secretory cells of the choroid plexus which is in communication with the lateral, third and fourth ventricles.CSF flows from the lateral ventricles to the third ventricle through the foramen of Monro and then into the fourth ventricle through the aqueduct of slyvius to then enter into the subarachnoid space of the spina cord through the two lateral foramen namely foramen of Luchska and Megendie. The total volume of the spinal cord is about 150ml at any point of time and it is produced at the rate of 0.35-0.40 ml/min or 500-600 ml/day, with the turn over time being 5-7 hrs. Half of this volume is present intracranially while the rest is in the subarachnoid space into which the injected drug gets distributed (6)

CSF is an isotonic, aqueous medium with a composition similar to the interstitial fluid. The density of CSF at 37 C has a range of 1.0000 -1.0006 with a mean of 1.0003

g/liter.(7)(8) However, in humans CSF density is not uniform and varies with age, sex, pregnancy and illness.

CSF is not static and continuously oscillates with arterial pulsations; studies have indicated that the extent and duration of spinal anesthesia with isobaric bupivacaine depend on the CSF velocity.

Procedure:

Spinal anesthesia is given in the midline or paramedian area in the L3-L4 space or L4-L5 space, with the patient in the sitting, lateral or prone position. The layers that need to be penetrated are skin, subcutaneous tissue, supraspinous ligament, interspinous ligament, ligamentum flavum, duramater and arachnoidmater. Usually there are two pops felt, one while penetrating the ligamentum flavum and another while crossing the dura – arachnoidmater. Once the second pop is felt, a free flow of CSF is seen. This confirms the position of the needle in the subarachnoid space.

Pharmacology of local anesthetics:

For a successful spinal anesthetic procedure one requires to have a sound knowledge and understanding of the pharmacology of the local anesthetic administered in the subarachnoid space. Local anesthetic act by blocking the conduction of nerve impulses. The normal resting potential of a nerve is -60 to -70 mV resulting from a dynamic balance that exists between the ionic concentration gradients maintained by the Na+/K+ ATPase pump and the diffusion potential of ions, mainly Na+ and K+. When an action potential is generated the resting membrane potential reaches threshold potential, owing to the activation of Na+/K+ ATPase which pumps 3 molecules of Na+ extracellularly for 2 molecules of K+ intracellularly, creating an electrical field across the cell membrane.(9) The Na+ channel exists in three states: closed, active and inactive. Local anesthetics can block the channel in the active state as Na+ conduction occurs only during this state.(10)

Local anesthetic inhibition of Na+ currents increases with repetitive depolarization in a process called phasic block. Phasic block represents increased LA binding, either because more channels become accessible during depolarization or due to the channel conformations favored by depolarization bind LA with higher affinity.

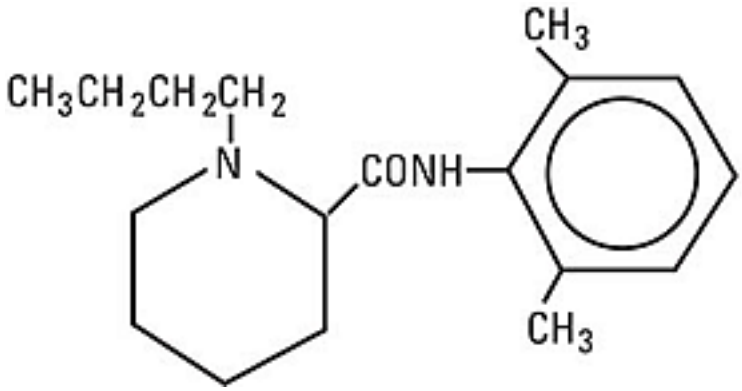
Thus, local anesthetic solutions cause reversible blockade of the impulse propagation in a manner that is both time and voltage dependant, resulting in increased threshold for activating the action potential. The clinically useful LA have a lipophilic, substituted benzene ring linked to a hydrophilic amine group via an ester or amide linkage, this linkage results in two chemically distinct groups namely the amino amides and the amino esters.

Local anesthetic potency, speed of onset, duration of action is determined by the dissociation constant pKa, lipid solubility and degree of protein binding.

BUPIVACAINE:

GROUP: Amino amide

CHEMISTRY:



SYSTEMIC NAME:

(RS)-1-butyl-N-(2,6-dimethylphenyl)piperidine-2-carboxamide

CHEMICAL FORMULA:

$C_8H_{28}N_2O$

MOLECULAR WEIGHT: 288.43g/mol

PHARMACOKINETICS:

Protein binding: 95%

Lipid solubility: highly lipid soluble

% ionized at pH 7.4: 83%

Metabolism: liver.

Excretion: kidney

Elimination half life: 3.5 hrs

Toxic dose: 2 mg/kg

Toxic plasma concentration: >3mcg/ml

CVS: CNS ratio is 2.0

It is more cardio toxic than other local anesthetics.

DETERMINANTS OF CLINICAL EFFICACY OF SPINAL ANESTHESIA:

The extent of sensory and motor blockade due to spinal anesthesia depends on the distribution of the local anesthetic drug within the sub arachnoid space and its uptake by the neuronal tissues determines which neuronal function is affected. The duration of action of spinal anesthesia depends on elimination half life of the local anesthetic agent used.

There are a number of factors that affect the distribution of the local anesthetics in the sub arachnoid space, the most important of them being the baricity of the drug and the dose of

the local anesthetic.(11) The position of the patient immediately after the spinal anesthetic drug administration is also of utmost importance.(11–15)

Authur E Baker was one of the first investigators to write a report on his experience with spinal anesthesia in 100 cases, in which he dealt with the factors affecting spinal anesthetic spread.(16) Almost about a century ago he discussed the effect of gravity, the influence of the lumbosacral curves and the possibility of increasing the baricity of the anesthetic drug by adding dextrose as some of the factors affecting the spread of the local anesthetic agent.

Factors affecting intrathecal spread of LA:(17)

Patient factors	Drug factors	Technique
Age Height Sex Curvature of the spine Lumbosacral CSF volume Pregnancy Intra abdominal pressure	Baricity Drug dosage Viscosity Additives Temperature	Patient position • During and • Immediately after the procedure Site of injection Needle type and direction Fluid currents Intrathecal catheters

Baricity:

It is the specific density of the anesthetic agent to the specific density of the CSF at 37^{o}C. The specific density of the CSF is 1.003-1.008 at 37^{o}C. Hence the drug injected into the subarachnoid space can be hyperbaric, isobaric or hypobaric compared to the CSF.

In clinical practice the most commonly used baricity is the hyperbaric solutions i.e) they are heavier/ denser than the CSF. So these solutions tend to settle at the most dependent part of the subarachnoid space and this helps in limiting the spread of CSF. In the lateral position a hyperbaric solution will settle down to the dependent side and thereby produce a greater effect on that side. When an isobaric solution is injected into the subarachnoid space it tends to remain at the level of injection whereas a hypobaric solution tends to move cephalad.(17, 14, 18)

Any local anesthetic solution can be made hyperbaric by adding dextrose or hypobaric by adding sterile water to it. As it is evident that the anesthetic solutions depend on gravity for their extent of spread, the patient position during and immediately after the spinal is of major importance as it determines the point of action of gravity.(19, 20)

Volume/dose:

Dosage of the anesthetic agent is also one of the most important factors in determining the extent of spread. In general, higher the dose of the agent greater the extent of spread. Most of the studies that have been done comparing the effects of dose and volume, the dose is the one that matters. On comparing volume and concentrations it was seen that if the volume is kept constant and different concentrations were used, by the end of 20 minutes all the groups showed similar concentration of the drug in the CSF.(22–27)

Additives:

When an additive like an opioid or α agonist is added to the local anesthetic agent and administered into the subarachnoid space, it prolongs the duration of action of the local anesthetic agent. Some of the commonly added additives are fentanyl, morphine and clonidine.(28)

CLINICAL TECHNIQUE:

Patient position:

Spinal can be given in the sitting, lateral and prone position. Spinal anesthesia can be localized to the side of surgery on the lower limb by keeping the patient in that position for 5- 10 minutes. Making a patient sit for 5 minutes after administration of the spinal anesthetic agent produces a saddle block. Studies have shown that position of the patient immediately after administering the drug is one of the important factors because of the interplay between density and patient position.(12, 26–29)

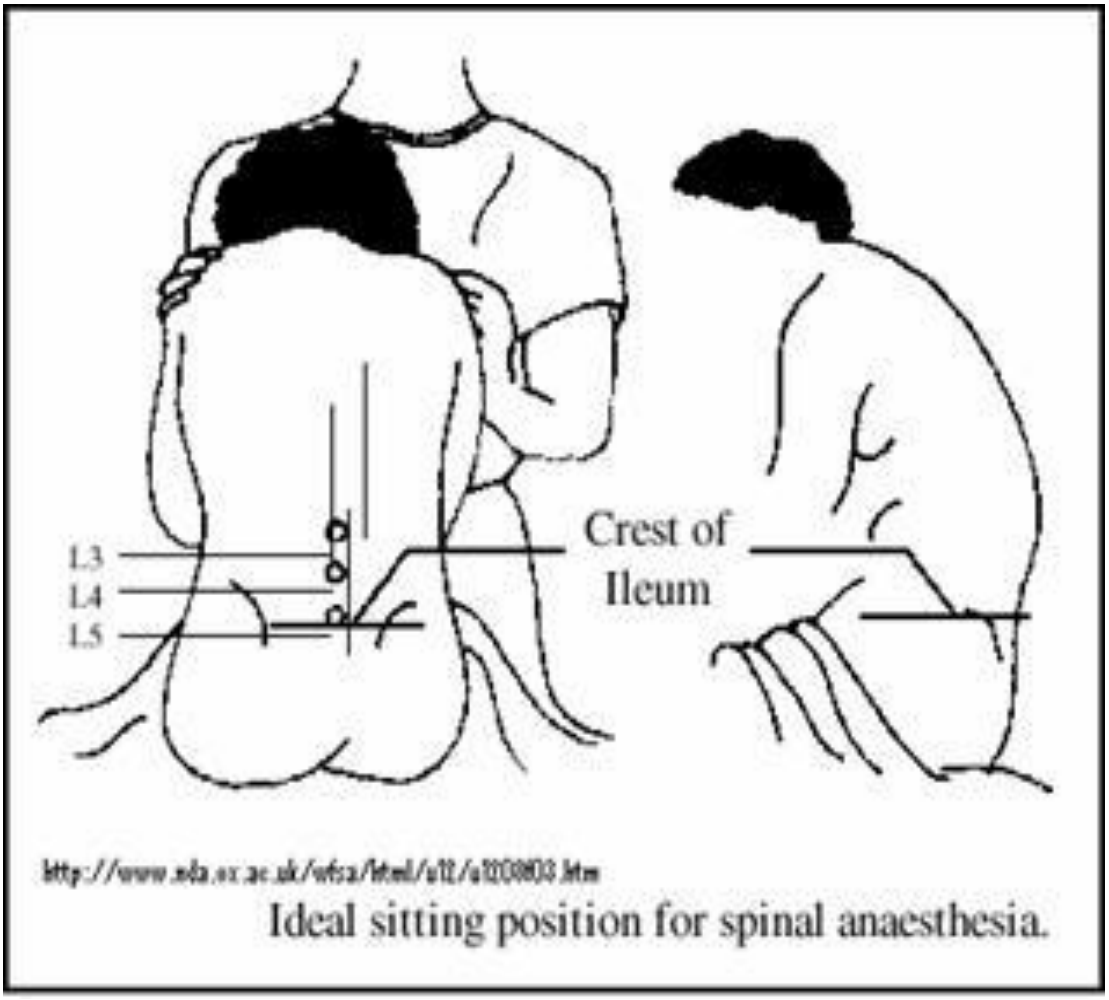


FIGURE 4: IDEAL SITTING POSITION FOR SPINAL ANESTHESIA.

Level of injection:

The higher the level of injection the greater the extent of spread of spinal anesthesia is the general phenomenon that is seen with plain solutions and less often with hyperbaric solutions.(32)

PATIENT CHARACTERISTICS:

Age, Height, Weight and sex:

In the older age group, there seems to be a significant increase in maximum spread, rate of onset and sometimes cardiovascular instability regardless of the solution used. These may occur secondary to changes in spinal anatomy, physiological changes that are associated with ageing in the central and autonomic nervous system.

Over the years it has been studied and concluded that shorter patients require lesser volume as the dose required per segment is lesser. Greater weight and BMI seem have an effect on the level of spread of spinal anesthesia as the epidural fat is considered to compress the dural sac resulting in decrease in CSF volume and a higher cephalad spread.(8)(33)

Hence a height and weight adjusted dose seemed to result in a favorable outcome with adequate level of sensory and motor anesthesia with advantages like decrease in hypotensive episodes and post operative nausea and vomiting.

ASSESSMENT OF SPINAL BLOCK:

The different methods used in assessing the degree or height of spinal block use the loss of motor and sensory functions as an indirect indicator. There are various types of nerve fibers and each of them has different features. The preganglionic B fibers carry autonomic impulses while the C fibers carry post ganglionic sympathetic nerve fibers, both of these are more sensitive to blockade by local anesthetic than the A fibers.

The A fibers are further divided into α,β,λ and δ which carry proprioception, touch, pressure, light touch and motor fibers respectively. Of these A λ is the largest in diameter and are more difficult to block. The variation in response to local anesthetics result in a differential blockade, clinically this translates as different levels of neutral blockade, clinically this translates as different levels of neural blockade, autonomic nerves are blocked at a higher level than the sensory which in turn is blocked at a higher level than motor nerves, these are generally separated by 2 segments. In practice, height of the block is checked starting from a non anesthetized area by the response to temperature or pinprick while motor block is assessed by using modified Bromage scale as follows:

Modified Bromage score as used by Breen et al for motor blockade assessment:

Score	Criteria
1	Complete block (unable to move feet or knees)
2	Almost complete block (able to move feet only)
3	Partial block (just able to move knees)
4	Detectable weakness of hip flexion while supine (full flexion of knees)
5	No detectable weakness of hip flexion while supine
6	Able to perform partial knee bend

PHYSIOLOGIC EFFECTS OF SPINAL ANESTHESIA:

Spinal anesthesia results in temporary symphathetectomy due to the blockade of the thoraco lumbar segments of the spinal cord that is responsible for the sympathetic outflow. This results in a decrease in blood pressure and heart rate.

The decrease in blood pressure results from a combination of decrease in venous return that serves to decrease preload and cardiac output and dilatation of the peripheral vessels which results in a drop in systemic vascular resistance. The arterial dilatation occurs due to a decrease in the level of circulating catecholamines due to blockade of sympathetic supply to the adrenals and the nerves that directly supply the blood vessels. Higher incidence of hypotension with spinal anesthesia is seen in case of higher cephalad spread, dural puncture above the level of L2L3 and in cases where a combination of general and spinal or epidural anesthesia is required.

Decrease in heart rate that is witnessed is due to the imbalance in sympathetic and parasympathetic systems. Decrease in pulse rate can occur either due to the direct effect of blockade of sympathetic fibers supplying the heart T1-T4 or due to the over activity of the parasympathetic system. Adequate preload is necessary to reduce the chance of bradycardia due to spinal anesthesia.

CARDIOVASCULAR EFFECTS

The dilatation of the resistance and capacitance vessels due to sympathetic blockade that results in hypotension is one of the common effects of spinal anesthesia on the cardiovascular system. High sympathetic blockade that blocks the cardiac accelerator fibers in combination with vasodilatation of the venous capacitance vessels leading to

decreased cardiac output can cause profound hypotension. Another common side effect that is witnessed is the decrease in heart rate. Both these side effects can be treated usually by using vasopressor and sympathomimetic drugs like atropine. Usually the effects of sympathetic blockade witnessed are directly related to the level of anesthesia achieved.

RESPIRATORY EFFECTS

In case of a higher level of sympathetic blockade which includes the upper abdominal muscles, the ability of a person to cough and clear secretions is impaired. This effect is exaggerated in people with severe chronic lung disease as they may be dependent on their accessory muscles of respiration like the abdominal muscles. Otherwise spinal anesthesia has minimal effects on the respiratory system when the level of anesthesia is limited to the lower limbs or the lower abdominal region.

CENTRAL NERVOUS SYSTEM EFFECTS

There are very minimal effects to the central nervous system except in case of high spinal anesthesia where the profound hypotension is attributed to the brain stem hypotension.

COAGULATION SYSTEM:

In the elderly population a fall resulting in a long bone fracture implies immobilization for a significant period of time which inturn increases the risk of deep venous thrombosis (DVT) and pulmonary embolism (PE). Being able to provide regional anesthesia in this age group provides the advantage of early mobilization and decreased hospital stay which inturn implies a reduction in the risk of DVT and PE.

AUTONOMIC NERVOUS SYSTEM:

The spinal anesthesia given in the lumbar region results in the blockade of the sympathetic outflow that is usually from the T5-L1 levels. This results in a decrease in the sympathetic tone and an increase in the parasympathetic tone.

COMPLICATIONS OF SPINAL ANESTHESIA:

HYPOTENSION AND BRADYCARDIA:

Decrease in blood pressure can be mild or severe in patients receiving spinal anesthesia depending on their volume status, level of sympathetic blockade, age and co morbidities. (34)The decrease in vascular resistance has been attributed as the cause for this fall in pressures. Severe hypotension is seen in cases of high spinal blockade, older patients and in hypovolemic patients.(35)(36) Pre loading the patient with intravenous fluids is shown to reduce the risk of hypotension. In patients with left ventricular dysfunction it is better to use continuous vasopressor infusion with lower volumes of fluid for resuscitation.(37)

The hemodynamic changes seen after spinal anesthesia are primarily due to the decrease in cardiac output and blood pressure though a decrease in heart rate also contributes to it. The incidence of severe bradycardia is about 1% and may lead to sudden asystole and cardiovascular collapse.(38)(39) Prompt treatment with atropine 0.5 to 1.0 mg and ephedrine 5 to 10 mg may prevent the progression.

Prompt treatment of hypotension and bradycardia, good pre loading of patient, vigilant monitoring and adequate replacement of blood loss during surgery prevents serious complications like cardiovascular collapse.

NERVE INJURY:

Persistent neurological deficit is one of the most dreaded but rare complications following spinal anesthesia and is usually due to direct nerve injury or due to drug toxicity. This can be prevented by injecting the drug below the level of the cord and reinserting the needle in case the patient complaints of persistent paraesthesia once the subarachnoid space is encountered.

Low backache radiating to the buttocks and back after successful reversal from a spinal anesthesia, is the usual presentation of a transient neurological symptoms (TNS). It can occur after 24 hours of spinal injection and last for a week. TNS usually occurs after the use of Lidocaine in spinal anesthesia. (40)(41)

POST DURAL PUNCTURE HEADACHE (PDPH):

PDPH is a constant or throbbing bifrontral or retro orbital and occipital headache that gets relieved on lying down but is aggravated in the upright posture. It is usually seen within a day or 2 of spinal anesthesia and resolves in about a week. Traction on the dura due to the loss of CSF from the dural defect of spinal anesthesia producing a decreased intracranial pressure has been sited as the reason for PDPH. Pregnancy, female sex and young age are some of the known risk factors.(42) Treatment is usually conservative with strict bed rest, generous administration of fluids, analgesics and caffeine containing solutions. In some cases the pain may become chronic and treatment with epidural blood patch may be required. Using a spinal needle of higher gauge can reduce the incidence of PDPH.(43)(5)(4)

TOTAL SPINAL ANESTHESIA:

When the level of sensory blockade with spinal anesthesia reaches above the cervical region, resulting in unconsciousness and respiratory paralysis in the patient, it is termed total spinal anesthesia. This usually occurs due to the unintentional accidental injection of a large volume of local anesthetic agent into the subarachnoid space while attempting an epidural. As the spread of the agent is in a large volume of CSF, the CSF concentration will be low and hence the resulting duration of action is short. Management is usually supportive with endo tracheal intubation and ventilation and vasopressor and ionotropes to support the decrease in blood pressure and heart rate.

HIGH SPINAL ANESTHESIA:

When the level of spinal blockade reaches the higher thoracic levels like T2 or cervical region resulting in paralysis of the intercostals muscles and the diaphragm without affecting the consciousness, it is called high spinal anesthesia. The patient may complain of dyspnea and usually has significant hypotension and bradycardia. Verbal reassurance and treatment of the hypotension and bradycardia is essential. Induction of spinal anesthesia after a failed epidural increases the risk of a high or total spinal anesthesia.(44)

LOCAL ANESTHETIC TOXICITY:

Extremely high levels of local anesthetic may be seen in the systemic circulation due to accidental intravascular injection and this can result in cardiovascular collapse and seizures. Hence it becomes important to aspirate and check if the needle tip is intravascular before administering the drug in case of spinal anesthesia. Transient

neurological symptoms and cauda equina syndrome can also occur very rarely with use of local anesthetics especially hyperbaric lidocaine.(40)

SPINAL HEMATOMA:

Rarely a large hematoma may occur following a spinal or epidural anesthesia that causes a mass effect by pressing down on the spinal cord leading to ischemia and direct pressure injury of the cord. A sudden onset backache radiating to the lower limbs and associated with motor or sensory deficits following the procedure should make one suspect an epidural or spinal hematoma. Early diagnosis using a magnetic resonance imaging or computed tomography and early surgical intervention can make a world of difference to the patient's neurological outcome.

CENTRAL NERVOUS SYSTEM INFECTIONS:

Asepsis during the spinal or epidural anesthetic administration becomes highly important as there is a possibility of causing meningitis, spinal or epidural abscess when contaminated equipments or local anesthetics are used or due to tracking in of bacteria from the skin.

OTHERS:

There are a number of other side effects that are seen very rarely with neuraxial anesthesia like urinary retention, high spinal anesthesia, total spinal anesthesia, cardiac arrest, anterior spinal artery syndrome, diplopia, tinnitus and backache.(45)

Review of Literature

REVIEW OF LITERATURE

Falls and long bone fractures are quite common in older people and most of them require surgical orthopedic procedures for stabilization of the bone and ambulation. With increasing age people seem to develop a number of co morbidities;(46) hence providing anesthesia to the older population becomes a challenge. Regional anesthesia is one of the preferred techniques of anesthesia for lower limb surgeries. Spinal anesthesia in the elderly is an excellent option compared to general anesthesia, as general anesthesia has a lot of problems which can be detrimental especially to the older population.(47)(48)

The disadvantages of general anesthesia are that when used with inhalation agents and intravenous agents it can cause direct cardiac depression effects, post operative delirium, increased blood loss, increased post operative nausea and vomiting especially due to opioid use, inadequate analgesia, delayed ambulation and longer hospital stay.(49)(50) On the other hand regional anesthesia has shown a number of benefits. Central neuraxial blockade like spinal or epidural anesthesia when compared to general anesthesia was found to decrease the incidence of complications like deep venous thrombosis (44%), pulmonary embolism(55%), transfusion requirements (50%), pneumonia (39%) and respiratory depression (59%), according meta analysis comparing regional and general anesthesia. According to this study the overall mortality was reduced by about 33% apart from a decrease in the incidence of myocardial infarction and renal failure.(51)

But one of the major problems associated with spinal anesthesia is hypotension, with the elderly age group displaying an exaggerated response.(52) (53)A significant decrease in blood pressure implies a significant decrease in mean arterial pressure, which inturn results in decreased organ perfusion, the result of which could be highly hazardous,

owing to the multiple co morbidities in the elderly. The exaggerated fall in pressures is mainly due to the decrease in systemic vascular resistance in the older age group.(54)(55) Reduced baroreceptor responses to fall in blood pressure and impaired autonomic activity have also been cited as the reasons for the exaggerated fall.(35)

Over the years anesthetists have tried different methods to reduce spinal hypotension some of them being, decreasing the dose, the baricity, preloading or co loading with crystalloids or colloids, etc.(56) Preloading in elderly may not be a wise thing to do, as they can have multiple co morbidities including cardiovascular problems which can result in cardiac failure. There are many factors that affect the spread, intensity and duration of spinal anesthesia but which factor carries more importance is the question that's on the mind of every anesthetist. Over the last few decades a number of studies have shown that dose of the drug injected was more important than the volume or concentration.

In the work done by LANZ et al in 1990, varying concentration and volume of isobaric bupivacaine were used while keeping the dose constant and they found no difference among the groups with regard to speed on onset, maximal spread, regression of sensory and motor block except in the group which received 10ml of 0.175% isobaric Bupivacaine where complete regression was faster, they however concluded that the dose was more important than either volume or concentration in isobaric Bupivacaine.(25)

A similar study by Malinovsky in 1999 compared different volumes of isobaric and hyperbaric Bupivacaine and he concluded that volume did not affect the extent of cephalad spread or duration of anesthesia but the offset of anesthesia was shorter with hyperbaric Bupivacaine compared to isobaric Bupivacaine.(26)

On analyzing a few other studies by authors like Thage et al concluded that dose is the most important factor. He also stated that in terms of hypobaric or isobaric solutions, baricity, age, weight and level of injection are also important. He felt spinal anesthesia resulted in a unpredictable sensory blockade.(27)

Teckelenburg-Weier et al one can conclude that the major factors affecting the spread of local anesthetic are the baricity of the solution and the position of the patient immediately after the spinal block.(57)

Fettes and Hocking et al on comparing different baricities of Ropivacaine in patients posted for elective perineal surgeries found a significant difference in the time of onset, maximum cephalad spread and duration of action.(58)

In our study 6ml of 0.25% of isobaric Bupivacaine was the study drug and 3ml of 0.5% hyperbaric Bupivacaine was the control drug. The total dose of the drug was kept constant at 15mg, as few studies suggested that that the dose of the local anesthetic drug is more important than the concentration or the volume.

The primary aim of our study was to evaluate if isobaric Bupivacaine provides more stable hemodynamics compared to hyperbaric Bupivacaine. This hypothesis was based on many studies especially the one by Nedim solakovic in 2010. He concluded that hyperbaric Bupivacaine produced significant drop in pressures compared to isobaric Bupivacaine and that isobaric Bupivacaine produced smaller deviation of the parameters.(59)

Veering et al studied the effects of hyperbaric bupivacaine in the sixty patients who underwent urological procedures under spinal anesthesia and were above the age of 65

years and found no difference in the maximum level of motor blockade and hemodynamic changes.(29)

Van Gessel et al 1991 also showed in their study comparing hyperbaric Bupivacaine with isobaric and hypobaric Bupivacaine during continuous spinal anesthesia that hyperbaric Bupivacaine produces greater hemodynamic changes compared to isobaric and hypobaric Bupivacaine solutions.(60)

Shimai N et al while studying the effect of hyperbaric and isobaric 0.5% solutions of Bupivacaine of different volumes showed that severe drop in blood pressure occurred with 0.5% hyperbaric Bupivacaine of greater volume. They finally suggested that adequate anesthesia with lesser drop in blood pressure could be obtained with a larger volume but lesser baricity of Bupivacaine or a lower volume with higher baricity.(61)

Phelan et al by their study comparing the efficacy of hyperbaric Bupivacaine 0.4% with isobaric Bupivacaine 0.5% in 67 patients showed that hyperbaric Bupivacaine resulted in a more rapid fall in pressures but had a more predictable dermatome level compared to isobaric Bupivacaine.(62)

Siaens et al compared three different solutions of varying baricities and dosages. Group 1, 2 and 3 received 10mg hyperbaric bupivacaine, 10mg of isobaric bupivacaine and 15mg of isobaric bupivacaine respectively. In the first two groups cephalad spread anesthesia duration, motor blockade and the decrease in mean arterial pressures were comparable. But group 3 had a higher cephalad spread, longer duration and more pronounced motor blockade, though the mean arterial pressures were comparable to the other groups.(19)

Yang et al studied sixty patients who received hypobaric, isobaric and hyperbaric bupivacaine 0.375% while undergoing hip or lower limb surgeries. He found a greater fall in mean arterial pressure and heart rate with the hyperbaric bupivacaine.(63)

Rama et al in 2002, in their work comparing hyperbaric, isobaric and hypobaric Bupivacaine found no difference in the hemodynamic changes, level of analgesia, degree of motor block or duration of anesthesia among the three groups.(64)

But Tattersall compared isobaric bupivacaine 15mg with hyperbaric Amethocaine (10-16mg) in 123 patients undergoing various surgeries. Patients who received isobaric Bupivacaine had a comparatively limited spread of analgesia that lasted longer associated with lesser hypotension.(65)

Roberts et al in a double blinded randomized control trial of 90 patients showed that hyperbaric Bupivacaine provided a more rapid and intense sensory blockade of intermediate duration while isobaric bupivacaine provided a longer duration of anesthesia with lesser block height and lesser cardiovascular disturbance.(66)

Rooke et al wanted to study the increased chance of hypotension in the older population leading to adverse side effects like myocardial infarction. So he included about fifteen patients with either previous myocardial infarction or stable myocardial ischemia or congestive heart failure and spinal anesthesia was given in these patients. The cardiac output, ejection fraction, mean arterial pressure and systemic vascular resistance were measured. Statistically significant decreases in cardiac output, ejection fraction, mean arterial pressures were noted. But cardiac function was found to be normal. Hence he concluded that the decrease in pressures were mainly due to decrease in systemic vascular resistance.(54)

Badner et al, studied the incidence of perioperative myocardial infarction (PMI) in 323 patients who were above 50 years of age and had cardiac disease posted for non cardiac surgeries and found that about 5.6% developed PMI which were mostly non q wave PMI on ECG.(67)

Slogoff and keats published an important article that included about 1023 patients who were studied for pre operative and intraoperative periods of hypotension and the incidence of myocardial ischemia post operatively. They found a threefold increase in PMI if pre operative hypotension was present and a eleven fold increase in PMI due to ischemic episodes during intra operative management.(68)

According to Charlson et al, patients who had persistent hypotension with MAP less than 20% for more than 60 minutes intra operatively ended up with serious ischemic cardiac complications. If the MAP was further reduced but their duration was less than 59 minutes they still ended up with greater number of cardiac complications. Hence he insisted on the importance of maintaining intraoperative blood pressure. Hence in case of persistent hypotension we started the patient on small dose of ionotropic support intraoperatively.(59)

Beattie et al did a meta analysis to see if the use of post operative epidural decreased the incidence of PMI. They found a difference in percentage of 3.8% in mortality rate between people who used epidural post operatively and those who didn't. Hence as post operative epidural use was found to decrease the incidence of PMI, we advocated the use of post operative epidural in our study.(70)

Rodgers et al in his study showed that the overall mortality and morbidity decreased in patients when neuraxial anesthesia like spinal or epidural anesthesia was used. There

were also reduction in serious side effects like myocardial infarction, renal failure, respiratory depression, pneumonia and thromboembolic episodes.(50)

Methodology

METHODOLOGY

A randomized control study was conducted on ASA I, II and III patients who were above the age of 60 years, posted for hip surgeries to study the effect of isobaric bupivacaine and hyperbaric bupivacaine given intrathecally in spinal anesthesia. The outcomes that we looked at were hemodynamic stability and adequacy of anesthesia. The sample size estimation was done based on a similar study by Van Gessel et al 1991. To detect a difference of 12% change of mean arterial pressure from baseline, assuming 15% standard deviation with 80% power and 5% level of significance the sample size was calculated to be 40 with 20 in each group.

The baricities of the solutions were analyzed and calculated for 37^{o}C in the department of Biochemistry in our institution. The baricity of the solution when mixed with distilled water was found to be 1.008 and so equal volume of hyperbaric bupivacaine solution and distilled water were mixed and used as the isobaric study solution.

AIM: To compare effect of spinal anesthesia with hyperbaric bupivacaine and isobaric bupivacaine in the elderly population, posted for hip surgeries.

DESIGN: Prospective randomized control trial.

INCLUSION CRITERIA: 1) ASA I, II & III

2) Patients more than 60 years of age

3) Patients posted for DHS and hemiarthroplasty

EXCLUSION CRITERIA: 1) ASA >III

2) Patients of age less than 60 years

3) Contraindications for regional anesthesia like deranged bleeding parameters, platelet count less than 75,000, increased intracranial pressure, infection at the site of spinal, patients with progressive neurological deficits, bleeding disorders intracranial tumors, spinal deformities and pre existing hypotension and fixed output states like aortic stenosis.

4) Patients with low GCS.

METHOD OF RANDOMIZATION: Randomization of the 40 patients was done using a computer generated block randomization process, to ensure equal allocation in each group. Sealed envelopes containing the numbers 1 and 2 were made after generating the random numbers from the computer.

Control group: received 3ml of 0.5% hyperbaric bupivacaine

Study group: received 6ml of 0.25% isobaric bupivacaine

For the study group 3ml of 0.5% bupivacaine was diluted with 3ml of sterile distilled water.

We were able to study a total of 31 patients who were randomized by a computer generated randomization, out of which 16 belonged to the control group and 15 belonged to the study group.

Procedure: Patients belonging to American Society of Anesthesiology physical status (ASA) class I, II & III will be randomly assigned to two groups 1 and 2 after taking their informed consent. An intravenous line was established either with an 18G cannula. Co-loading with 250ml of colloid was done in all patients to reduce the possible spinal hypotension and further fluids were given at the rate of 2ml/kg apart from replacement of blood loss. All patients received 6l/min of O_2 via the facemask.

Standard monitoring was done in both groups using electrocardiography, non invasive blood pressure measurement and pulse oximetry.

After recording the baseline heart rate, systolic and diastolic blood pressure and mean blood pressure the patient was positioned in the sitting posture and depending on the randomization the patient belonged to either group 1 or 2.The area of injection was cleaned and draped by the anesthetist following which an epidural catheter was first inserted at the L2-L3 level prior to spinal anesthesia in both the groups, after the identification of the epidural space by loss of resistance technique using a 18G Tuhoy needle.

FIGURE 5: STERILE TRAY WITH SPINAL AND EPIDURAL NEEDLES USED IN STUDY.

Patients belonging to group 1 received regional anesthesia by subarachnoid block with 0.5% hyperbaric bupivacaine 3ml (15mg) and patients in group 2 received 0.25% isobaric bupivacaine 6ml(15mg) at the L3-L4 level using a 25G Whittacre needle once the drainage of clear CSF was seen. The patient was then made supine within a minute of drug administration.

Intra operatively a patient's systolic, diastolic blood pressure, mean arterial pressure and heart rate were recorded every three minutes for the first half an hour and then every 5 minutes. A decrease in blood pressure of more than 20% of mean arterial pressure was considered as intraoperative hypotension and was treated with vasopressors like Ephedrine 5mg or Phenylephrine 100ug or in case of recurrent prolonged hypotensive

episode; an ionotropic infusion like Noradrenaline infusion was started. Motor blockade was assessed by modified Bromage scale and sensory blockade was assessed by using a frozen ice pack to evaluate the loss of temperature sensation.

Assessment and management:

Once the epidural catheter was put in place and the spinal anesthesia was given, the patient was made supine and the heart rate, systolic and diastolic blood pressure and mean arterial pressures were measured every five minutes for the next 2 hours.

Intra operatively all the patients were assessed for

a) Sensory level of anesthesia

b) Motor blockade

c) Time of onset of spinal anesthesia

d) Baseline pulse rate and blood pressure.

e) Blood pressure and pulse rate monitoring for the next 2hrs every 5 mins

f) Requirement of vasopressor or ionotropic supports.

Post operatively the patients are assessed for the following

a) Blood pressure and pulse rate.

b) Sensory level of anesthesia

b) Motor blockade of anesthesia

The epidural inserted was utilized for post operative analgesia, through continuous infusion of the local anesthetic drug, 0.1% bupivacaine with 2 ug/cc of fentanyl. It has a number of advantages like excellent analgesia, early ambulation, no risk of respiratory depression and post operative nausea and vomiting due to decrease in opioid requirement.

Results

RESULTS

Table 1: Number of males and females

SEX	Control N	Study N
Male	**10**	**6**
Female	**9**	**6**

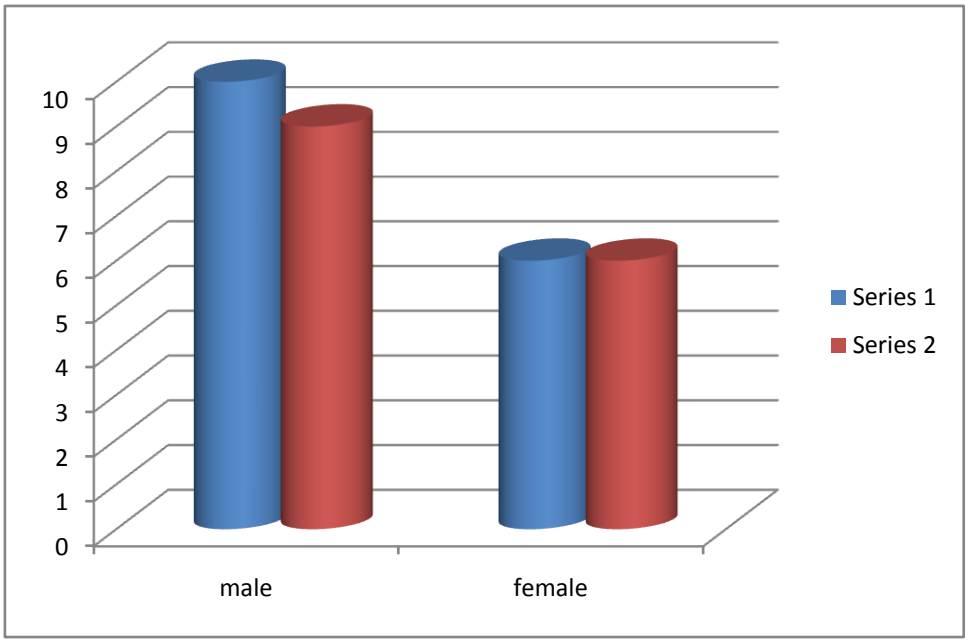


Figure 1: **Comparison of number of males and females**

The number of male and females in both the study and the control groups were comparable.

Table 2: Comparison of mean and SD of age and height.

PARAMETERS	CONTROL Mean±SD	STUDY Mean±SD
AGE	74.38± 8.60	70.93±7.21
HEIGHT	163.56 ±6.66	164.47±4.41

The age and height of patients in both the groups were comparable.

TABLE 3: Comparison of ASA risk status between control and study groups

ASA risk status	Control %	Study %
ASA I	37.5	20.0
ASA II	56.2	73.3
ASA III	6.2	6.7

The ASA risk status in both the groups were comparable and majority of the patients belonged to ASA status II.

TABLE 4: PRE OPERATIVE VITALS

Parameters	Control Mean± S.D	Study Mean± S.D
Systolic blood pressure	141.69±19.86	143.67±16.70
Diastolic blood pressure	76.50±9.07	76.80±7.80
Mean arterial pressure	95.69±9.04	96.00±9.55
Heart rate	93.75±13.22	91.47±16.15

The control and the study group were comparable in terms of age, sex, ASA risk stratification and pre operative value of blood pressure and heart rate.

TABLE 5: Distribution of surgeries between the two groups.

NAME OF THE SURGERY	CONTROL	STUDY
DYNAMIC HIP SCREW FIXATION (DHS)	81.2	73.3
HEMIARTHROPLASTY	6.2	20.0
PROXIMAL FEMUR NAILING (PFN)	12.4	6.7

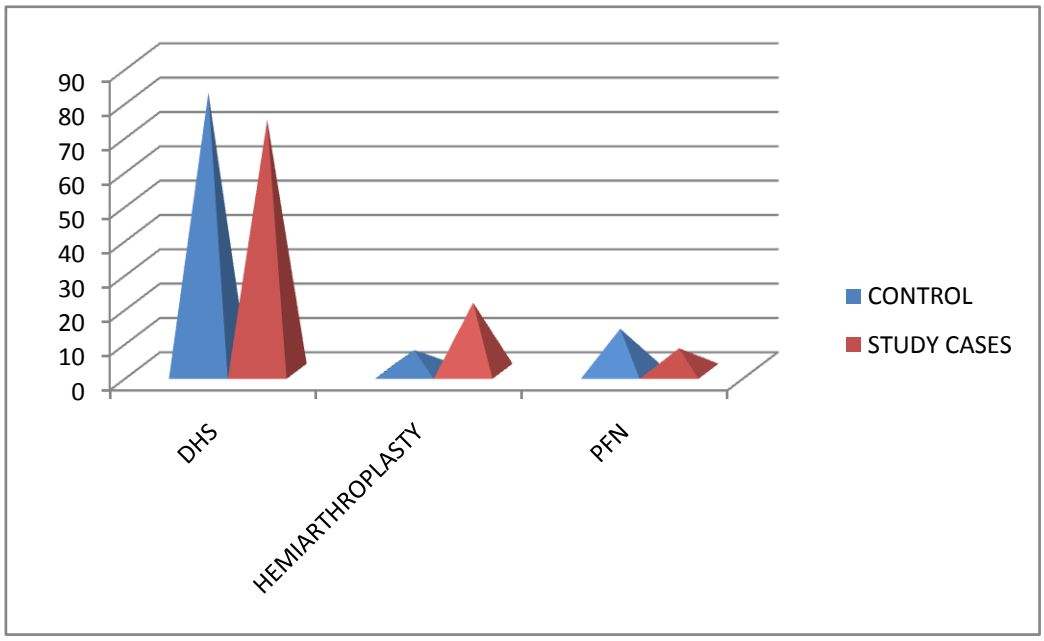


FIGURE 2: showing the distribution of surgery

Majority of the patients in both the control and study group had intertrochanteric fracture and were posted for dynamic hip screw fixation.

TABLE 6: TIME OF ONSET OF MAXIMAL CEPHALAD BLOCK

TIME OF ONSET IN MINUTES	CONTROL Mean±SD	STUDY Mean±SD	p value
AVERAGE TIME OF ONSET	3.4±1.23	2.8±1.06	0.141

The maximum cephalad spread took about 3.4minutes and 2.8 minutes in the control and study groups respectively but the difference was not statistically significant.

TABLE 7: AVERAGE DERMATOMAL SPREAD OF SENSORY ANESTHESIA

LEVEL OF SENSORY ANESTHESIA	CONTROL	STUDY
T4	1	0
T5	3	2
T6	6	6
T7	2	4
T8	2	1
T9	1	0
T10	0	2
T11	0	0
T12	1	0

The maximal sensory block was upto **T6** in both groups most often, which is higher than required, while the mean onset of spinal anesthesia was about **3.4** minutes among the controls and **2.8** minutes among the study cases.

The motor blockade after the onset of spinal anesthesia in both the control and the study group was grade 1 according to the modified Bromage scale.

This implies that we can probably reduce the dose of the drug as the maximal sensory block achieved is more than what is required.

Table 8: Average systolic blood pressure in both groups:

Time in mins	Control	Study	p value
5 mins	126±14.73	115.87±19.24	0.10
10 mins	110.38±24.92	107.80±19.03	0.75
15 mins	108.81±23.41	101.93±16.77	0.35
20 mins	103.19±19.81	109±20.68	0.42
30 mins	146.44±15.21	105.00±14.60	0.30
40 mins	161.75±18.20	108.20±22.03	0.35
50 mins	113.38±19.78	112.06±15.30	0.88
60mins	116.56±16.73	111.80±15.66	0.42
1hr 15 mins	117.88±17.42	116.53±16.72	0.82
1hr 30 mins	114.06±14.31	122.36±15.60	0.14
1hr 45 mins	120.71±18.81	124.36±20.45	0.64
2hrs	120.36±119.24	125.38±25.34	0.55

The majority of the hemodynamic changes were seen during the first 40 minutes after the spinal anesthesia. In this table the changes in systolic blood pressure are comparable in both groups because the study group needed vasopressor and ionotropes.

The maximum drop in pressure was seen at 20 and 15 minutes respectively in the control and study groups.

Figure 3: graph showing means of systolic pressure at 5 minutes interval over 2 hours

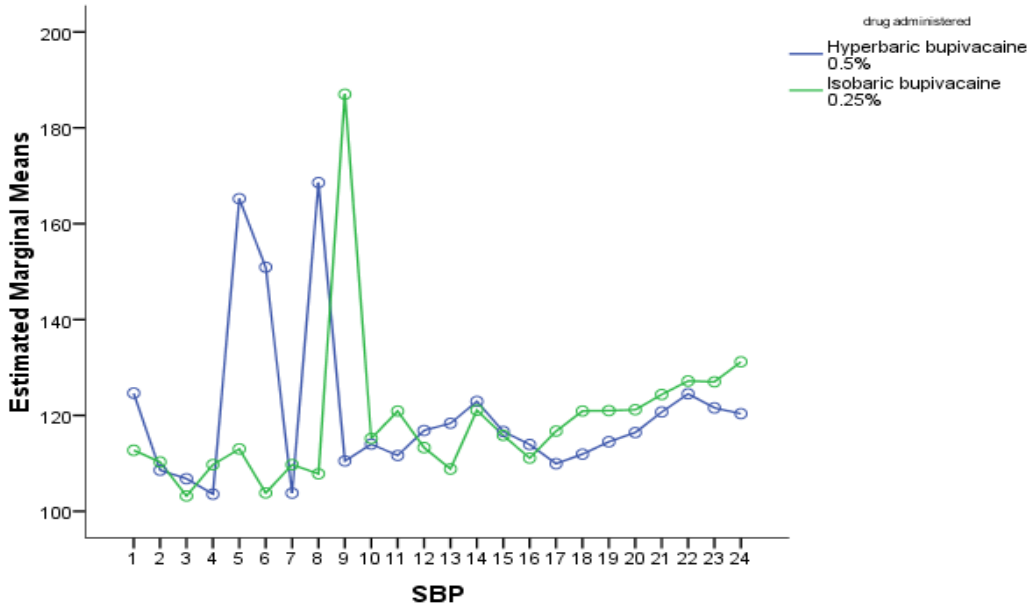


Figure 4: graph showing the means of diastolic blood pressure in the control and study group.

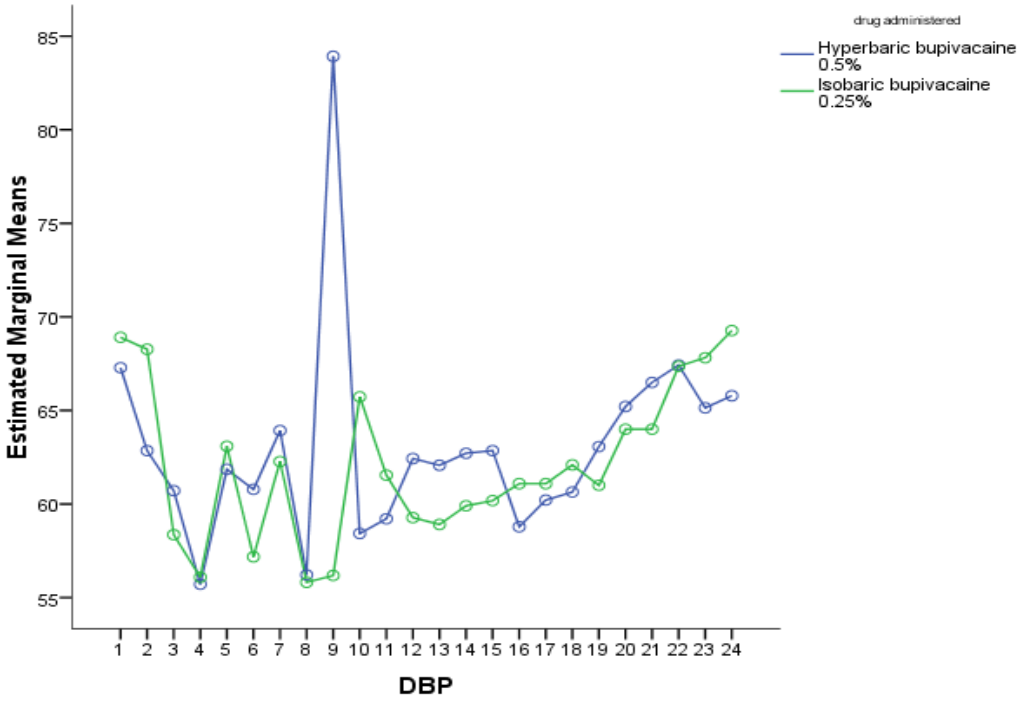


TABLE 9: AVERAGE DIASTOLIC BLOOD PRESSURE IN BOTH THE GROUPS.

Time in mins	Control	Study	p value
5 mins	67.88±13.12	65.87±15.41	**0.69**
10 mins	63.38±18.34	63.93±15.68	**0.92**
15 mins	61.19±13.98	58.33±15.77	**0.59**
20 mins	55.38±15.03	57.07±13.67	**0.74**
30 mins	59.38±22.12	57.40±12.55	**0.76**
40 mins	55.50±12.60	55.40±11.43	**0.98**
50 mins	57.56±9.81	63.53±17.35	**0.24**
60 mins	61.19±13.37	60.53±11.20	**0.88**
1hr 15 mins	62.19±11.47	63.07±13.91	**0.84**
1hr 30 mins	61.06±11.19	62.21±9.77	**0.76**
1hr 45 mins	66.50±13.54	64.00±13.60	**0.65**
2hrs	65.79±9.39	69.27±10.54	**0.39**

The diastolic blood pressure changes were also comparable in both groups and it was statistically insignificant at all time points. The trends were similar as any fall in pressures of more than 20% was treated in both groups.

Figure 5: graph showing the trends in mean arterial pressure in the control and study group

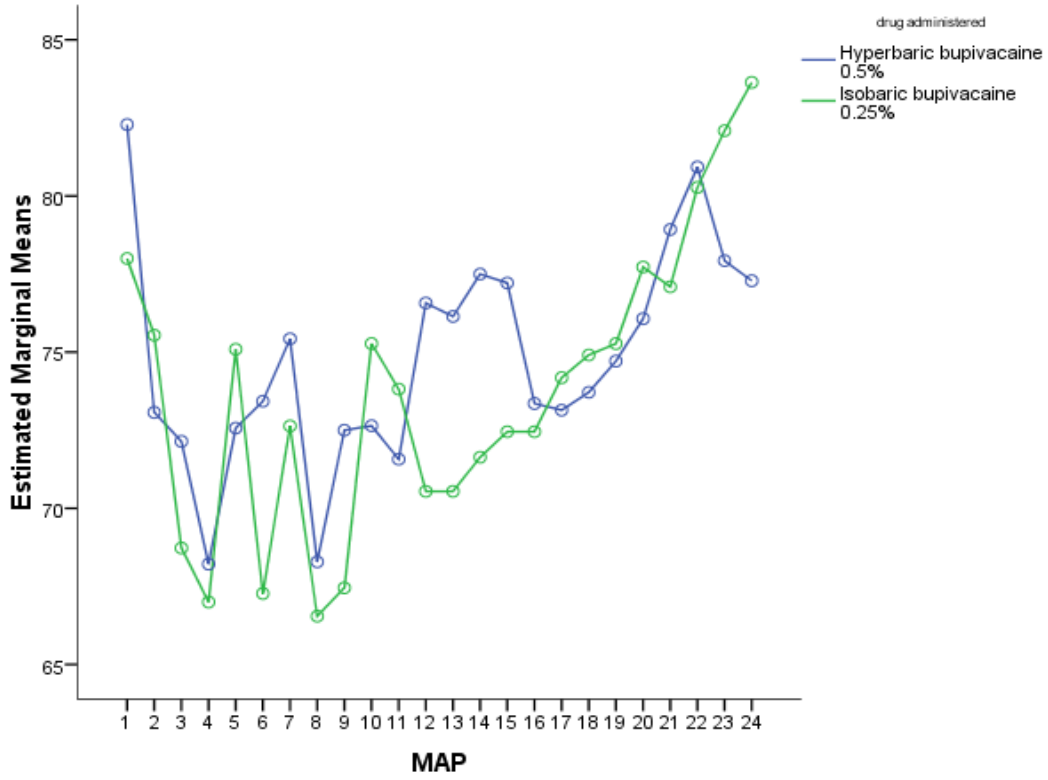


TABLE 10: AVERAGE MEANS OF MEAN ARTERIAL PRESSURE IN BOTH GROUPS

Time in mins	Control MEAN±SD	Study MEAN±SD	p value
5 mins	82.88±11.28	79.27±13.52	0.42
10 mins	73.62±19.79	73.47±13.63	0.98
15 mins	73.00±15.02	68.73±14.36	0.42
20 mins	67.62±16.12	69.00±13.54	0.80
30 mins	72.06±19.13	69.13±11.18	0.61
40 mins	68.00±13.92	68.40±10.20	0.93
50 mins	71.69±12.17	75.07±14.47	0.48
60 mins	75.31±13.08	72.60±9.49	0.51
1hr 15 mins	76.50±13.65	74.67±9.70	0.67
1hr 30 mins	74.06±11.38	76.79±9.83	0.40
1hr 45 mins	78.93±14.85	77.09±10.08	0.85
2hrs	77.29±10.07	83.64±10.55	0.40

The mean arterial pressures of both groups were also comparable but statistically insignificant in both groups.

FIGURE 6:graph showing the trends in Heart rate in the control and study groups

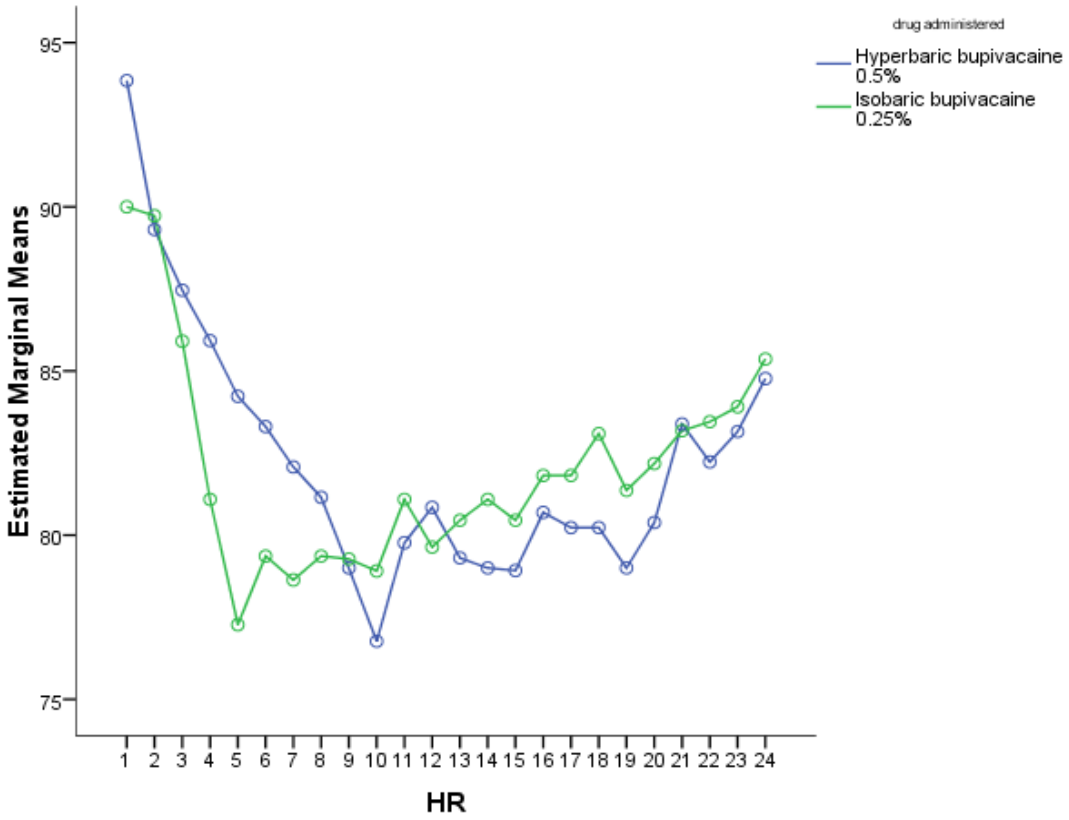


TABLE 11: AVERAGE HEART RATE IN BOTH GROUPS

Time in mins	Control	Study	p value
5mins	93.25±14.45	90.47±16.09	0.61
10 mins	89.88±13.00	89.60±15.74	0.96
15 mins	88.56±13.73	85.67±13.32	0.55
20 mins	86.62±12.9	81.80±15.1	0.35
30 mins	84.00±13.11	80.00±12.29	0.39
40 mins	82.81±13.15	79.93±13.26	0.54
50 mins	79.06±14.04	78.33±14.70	0.89
60 mins	82.31±12.38	79.40±13.82	0.54
1hr 15mins	81.06±12.03	81.20±15.74	0.98
1hr 30 mins	82.38±14.45	83.71±17.50	0.82
1hr 45 mins	83.71±12.56	83.18±17.10	0.93
2hrs	84.77±133.03	85.36±19.09	0.93

The changes in heart rate observed were comparable in both groups and no episodes of significant bradycardia were noted,

TABLE 12: NUMBER OF PATIENTS WHO REQUIRED NORADRENALINE INFUSION

No of patients	Control	Study cases	p value
Nor Adr required	10	2	0.005(significant)
No Nor Adr required	6	13	

The hyperbaric bupivacaine group required Noradrenaline infusion much more than the isobaric group and this was found to be statistically very significant.

FIGIURE 7: showing the number of people who needed nor adrenaline infusion.

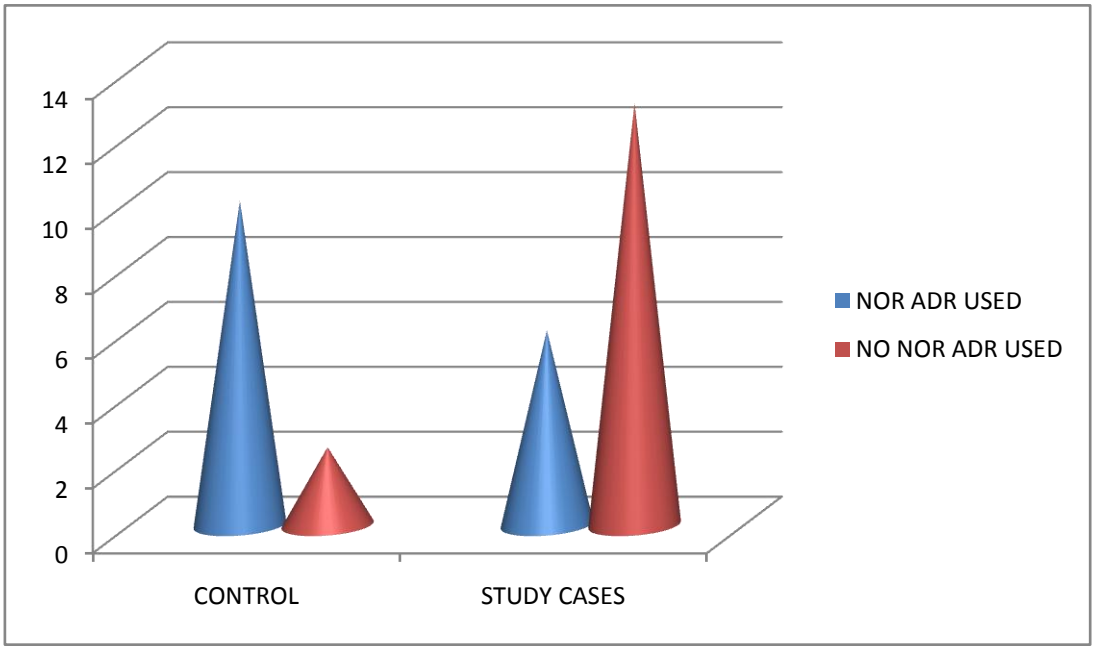


Table 13: Comparison of incidence of hypotension between the two groups

Parameters	Control N	Study cases N	p value
Hypotension	**11**	**2**	**0.002(significant)**
Nil	**5**	**13**	

The hypotensive episodes were much higher with the 0.5% bupivacaine than the 0.25% isobaric group and it was statistically significant

FIGIURE 8: showing the incidence of hypotension between the two groups

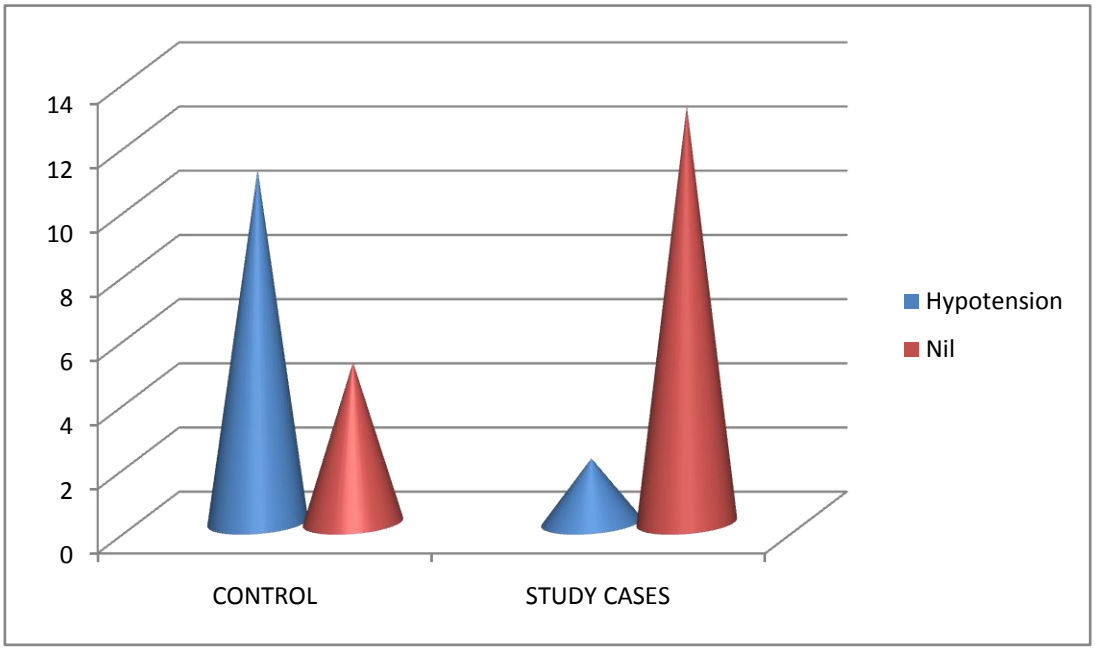


Table 14: Need for intraoperative epidural activation.

No of patients	Control	Study cases	p value
Yes	**5**	**3**	**0.685**
No	**11**	**12**	

A few patients required epidural infusion due to either inadequate sensory or motor blockade in both groups and it was found to be statistically insignificant.

FIGIURE 9: showing the intraoperative epidural activation.

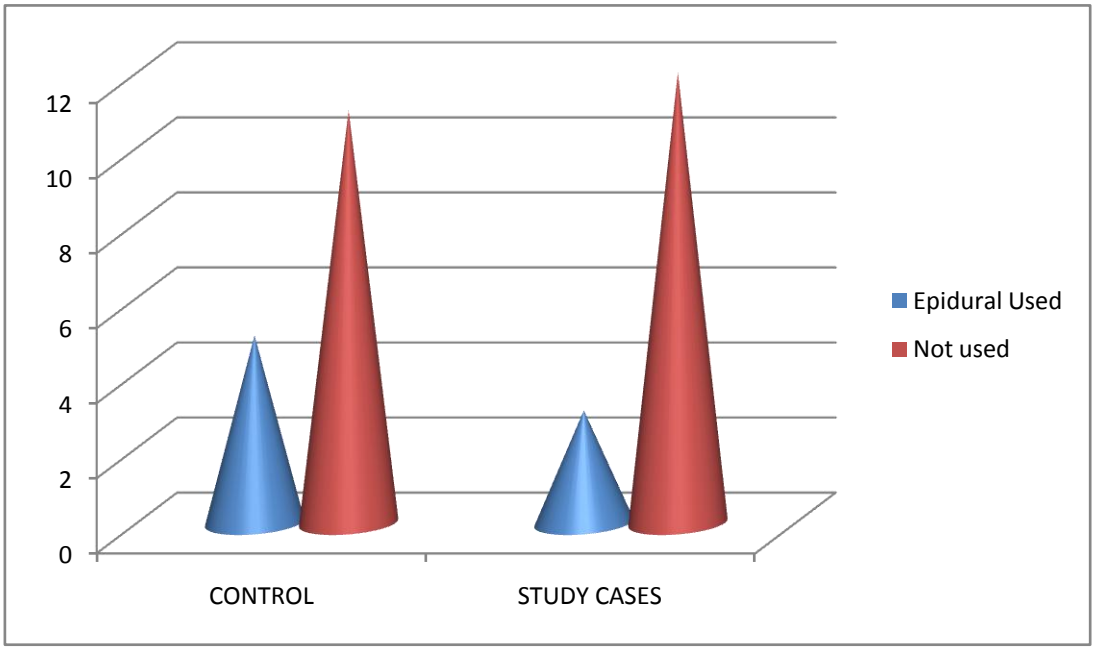


TABLE 15: REASONS FOR EPIDURAL ACTIVATION.

No of patients	Control	Study cases	p value
Inadequate sensory blockade	**3**	**2**	**1.000**
Inadequate motor blockade	**2**	**1**	

TABLE 16: AVERAGE DURATION OF ACTION

Duration in hours	Control	Study cases	p value
Time	**3.04±0.81**	**2.38±0.10**	**0.053**

Though their seemed to be a difference in average duration of action of approximately 25 mins it was not statistically significant.

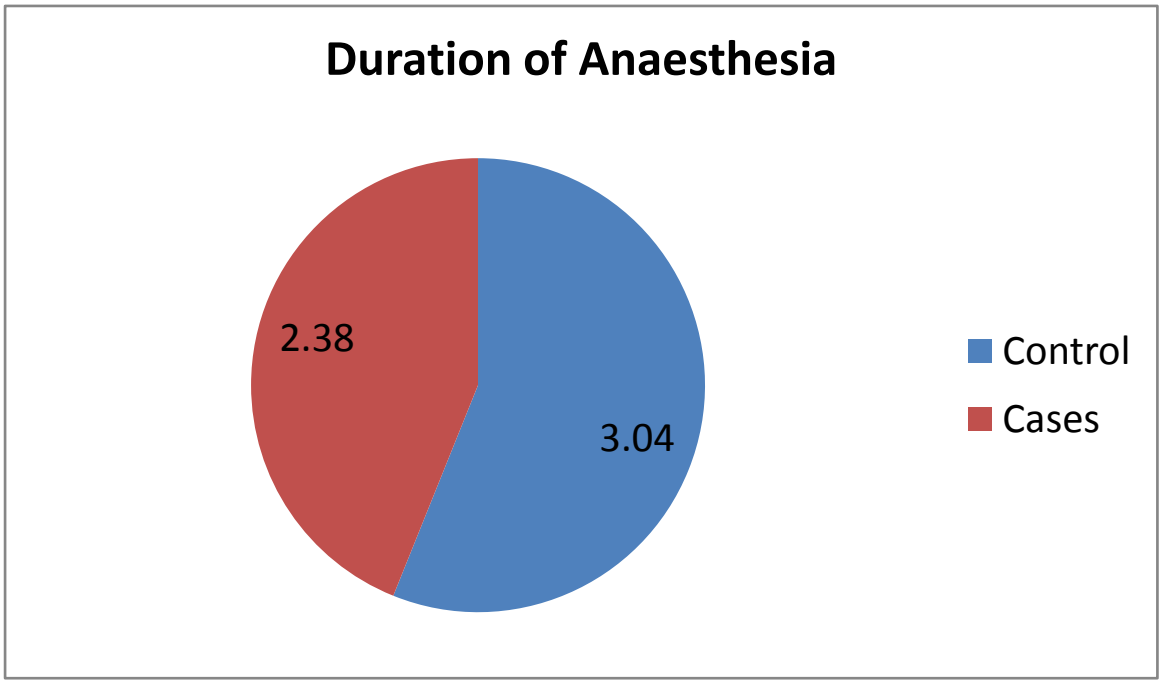


Table 17: comparison of overall complications

Complications	**Control N (%)**	**Study N (%)**	**P value**
Hypotension	11 (61)	2 (12)	**0.001(significant)**
Inadequate motor blockade	2 (11)	1 (6)	
Inadequate sensory blockade	3 (17)	2 (12)	
Nil	2 (11)	12 (71)	

The overall complication rates observed were also much higher with the hyperbaric bupivacaine group.

TABLE 18: HEMODYNAMICS IN THE RECOVERY

Parameters	Control Mean±SD	Study cases Mean±SD	p value
Systolic blood pressure	127.50±17.37	132.60±16.60	0.411
Diastolic blood pressure	72.88±14.69	69.27±8.23	0.404
Mean arterial pressure	86.50±15.16	87.40±11.11	0.853
Heart rate	93.00±17.29	96.00±18.55	0.645

The mean blood pressures and heart rate of the patients in the recovery were measured and analyzed. It was comparable but statistically insignificant.

TABLE 19: SENSORY LEVEL SEEN IN RECOVERY.

Level	Control N (%)	Study cases N (%)
T6	0 (0)	1 (7)
T8	2 (12)	0 (0)
T10	6 (38)	4 (27)
T11	1 (6)	2 (13)
T12	3 (19)	5 (33)
L1	1 (6)	1 (7)
L2	3 (19)	2 (13)

When the sensory level was checked in recovery most of the patients in both groups were within the T10-T12 level. Hence the sensory blockade was adequate with both groups in most cases.

Table 20: Motor blockade seen in recovery (according to modified Bromage scale)

Bromage scale grade	Control	Study cases
1	**2 (12)**	**2 (13)**
2	**6 (38)**	**5 (33)**
3	**3 (19)**	**5 (33)**
4	**2 (12)**	**1 (7)**
5	**0 (0)**	**1 (7)**
6	**3 (19)**	**1 (7)**

Hence from the table it is obvious that majority of the study cases had a motor blockade of grade 1 to 3, that they were probably able to just about move their knees. While in the control group majority of the patients belonged to grade 1 -4, with a few people being able to perform partial knee bend. This implies that 0.25% bupivacaine provides a much denser block compared to 0.5% bupivacaine.

Discussion of Results

Discussion of results

Elderly patients are to prone to higher intra operative and post operative morbidity and mortality compared to young patients. This can be attributed to the higher incidence of co morbidities in the elderly population. Falls and long bone fractures in the elderly are quite common and most of them require surgical orthopedic procedures for stabilization of the bone and ambulation. Regional anesthesia is one of the preferred methods of anesthesia in the elderly.(51,52,54) It is preferred over general anesthesia as general anesthesia with inhalation agents and intravenous agents can cause direct cardiac depression effects, post operative delirium, increased blood loss, increased post operative nausea and vomiting especially due to opioid use, inadequate analgesia, delayed ambulation and longer hospital stay. One of the most common cardiovascular side effect of regional anesthesia is hypotension and the elderly population are found have an exaggerated fall in blood pressure compared to the normal population and it is mainly due to the decrease in systemic vascular resistance. Reduced baroreceptor response to fall in blood pressure and impaired autonomic activity has been cited as the reasons for the exaggerated fall. An exaggerated fall in blood pressure implies decreased perfusion of already compromised organ system due to the multiple co morbidities that is usually seen in the elderly resulting in hazardous outcomes.(71) Hypertensive patients also seemed to show a greater fall in blood pressure. A number of studies have shown that pre morbid conditions and intra operative management can affect the incidence of complications like postoperative myocardial infarction (PMI).(68)(67) In 2000 Priebe et al concluded that there is higher possibility of cardiac risk with increasing age of the patient.(46)

This study was conducted in people aged more than 60 years coming for hip surgeries following femur fractures. Majority of the patients in both the control and the study group

were posted for dynamic hip screw (DHS) fixation surgery, with a few patients being posted for hemiarthroplasty and proximal femur nailing (PFN). Out of the 31 patients studied majority of them belonged to ASA risk status II, which is about 60-70% of the patients in either group. This implies that majority of the patients included had one or more co morbidities. These surgeries lasted anywhere between 90 minutes to 330 minutes, so while giving spinal anesthesia one has to consider a drug that would provide adequate analgesia and motor blockade for that time duration, without producing much of a hemodynamic instability. Hence providing anesthesia in this age group was nothing short of a challenge.

The aim of the study was to find out if isobaric bupivacaine or hyperbaric bupivacaine produces the most stable intraoperative hemodynamics. The incidence of hypotension was much less with isobaric bupivacaine and it was also statistically significant (p value of 0.002). In both groups the first 40 minutes of the procedure was when the majority of the chances in blood pressure and heart rate occurred. The mean of systolic blood pressure, diastolic blood pressure, mean arterial pressure and heart rates were comparable but they were not statistically significant.

This is in keeping with the solakovic et al, Van Gessel et al and Simai et al who found a greater fall in blood pressure and heart rate with hyperbaric bupivacaine when compared to isobaric bupivacaine.(59,60)(61)

Siaens et al, phalen et al, Roberts et al and tattersall et also seemed to show a lesser fall in blood pressure with isobaric bupivacaine.(19,62,65,66)

Rama et al, though they didn't find a significant difference between the two groups in causing hypotension and similar to our study there was no difference in the level of sensory and motor blockade achieved once spinal was given.(64)

They also didn't seem to have any significant decrease in the maximal level of spread and onset of action except for tattersall et al who showed that there was limited spread of analgesia with isobaric spinal anesthesia.

Siaens et al also showed that there was no difference between the hyperbaric and isobaric groups that were given the same dose in terms of level of analgesia and motor blockade but the third group where an increased dose of isobaric agent was given showed a higher level of spread.(19)

A fall in systolic blood pressure of more than 20% from baseline was defined as hypotension and it was treated with ephedrine in 5mg boluses and Phenylephrine in 100μg boluses. But if persistent hypotension was noticed then ionotropic support with single strength noradrenaline infusion was started, as it can cause a number of severe adverse effects like postoperative MI especially in the elderly.(69) Though the consumption of vasopressor like ephedrine and Phenylephrine was not significant, the need to start ionotropic support was statistically significant with a p value of 0.005. Hence from the results obtained we can conclude that isobaric bupivacaine produces a more hemodynamically stable intraoperative period in the patients aged more than 60 years.

The secondary outcomes that we looked at were adequacy of motor and sensory blockade produced by these two drugs, hyperbaric and isobaric bupivacaine. The time of onset and maximal cephalad block seemed to be similar in both groups. Most patients achieved a

block height of about T6 that is more than adequate for surgery of the hip. Hence we can probably reduce the dose of the drug.

The levels of sensory and motor blockade were measured at the end of the surgery in the recovery room which also seemed to be adequate in most patients only a few patients needed epidural to be activated intraoperatively in view of inadequate sensory or motor blockade and it was statistically insignificant. There was only one patient who needed conversion to GA as she become extremely restless during the surgery. One of the major limitations of this study was the inclusion of only a few patients.

Conclusion

Conclusion

Hemodynamic stability during the intraoperative period is important to prevent serious adverse effects like post operative MI especially in the aging population.

Compared to 0.5% hyperbaric Bupivacaine 0.25% isobaric Bupivacaine provides better hemodynamic stability and decreases the incidence of complications like hypotension and the need for ionotropic support.

Hence we recommend the use of 0.25% isobaric Bupivacaine in the elderly, who have multiple co morbidities and a higher incidence of adverse cardiac events in the perioperative period.

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Proforma

Data collection sheet BARGER study : **SERIAL NO:**

Comparision of hyperbaric bupivacaine versus isobaric bupivacaine in elderly patients

Name of the patient:

Age:

Sex:

Height of the patient:

Drug administered : 1/2

Hospital no:

Name of the procedure:

Diagnosis:

Baseline BP:

Baseline MAP:

Baseline PR:

TIME OF SPINAL:

Onset of action of spinal:

Sensory level:

Motor blockade:

Duration of the procedure:

TIME	5min	10min	15min	20min	25min	30min	35min	40min	45min
SYS BP									
DIAS BP									
MAP									
% DEC IN BP									
VASO REQ									
HR									

TIME	50min	55min	60min	1h5min	1h10min	15min	20min	25min	30min
SYS BP									
DIAS BP									
MAP									
% DEC INBP									
VASO REQ									
HR									

TIME	35min	40min	45min	50min	55min	2hr			
SYS BP									
DIAS BP									

MAP									
% DEC IN BP									
VASO REQ									
HR									

Need for epidural: yes/no bolus:

Time to recovery room:

Blood pressure:

MAP:

Heart rate:

Sensory level:

Motor blockade:

Complications:

Comments if any:

Modified Bromage score as used by Breen et al for motor blockade assessment:

Score	Criteria
1	Complete block (unable to move feet or knees)
2	Almost complete block (able to move feet only)
3	Partial block (just able to move knees)
4	Detectable weakness of hip flexion while supine (full flexion of knees)
5	No detectable weakness of hip flexion while supine
6	Able to perform partial knee bend

Consent sheet for men and women participating in BARGER study.

Informed consent sheet no: department of anesthesia, Christian medical college.

Title: Comparative study of isobaric bupivacaine versus hyperbaric bupivacaine in patients aged more than 60 years posted for hip surgeries.

Person performing study: Dr. Juliana Josphine. J

INFORMATION SHEET

PART I:

INTRODUCTION: I am Dr. Juliana Josphine. J, currently doing my M.D anesthesia, postgraduate training in Christian medical college, vellore. I am doing a study comparing the hemodynamic effects of isobaric bupivacaine with hyperbaric bupivacaine in elderly patients undergoing hip surgeries. I will be giving information about this study and invite u to take part in the same. Your decision to take part in the study need not be made today itself and also u are welcome to talk to anyone about this study. If u have any queries regarding the study please ask me and I will explain it to u. If u have any doubts later, u can ask me or your anesthetist on the day of your surgery.

PURPOSE OF THE STUDY: To compare the effectiveness of isobaric bupivacaine to hyperbaric bupivacaine, in terms of stable blood pressure and heart rate in the elderly population coming for hip surgeries.

PARTICIPANT SELECTION: More than 50 yr old patients, ASA I, II and III, posted for hip surgeries.

INFORMATION REGARDING THE STUDY: Patients participating in this study will receive combined spinal epidural injection at the beginning of the case. Either 0.5% hyperbaric bupivacaine 3ml or 0.25% isobaric bupivacaine 6ml will be given into the spinal fluid. An epidural catheter will put in place but will be activated only if necessary, This drug has been approved by FDA (Food and Drug Administration, USA) and DCGI (Drug Controller General India).

PROCEDURE AND PROTOCOL: you will be brought to theatre half an hour before the procedure and you will be positioned in sitting position once an IV line has been secured. The lumbar vertebral spaces l2-l3 and l3-l4 will be identified. After cleaning and draping the area, local anesthesia will be provided in the above mentioned spaces in the midline using 2% Lignocaine. Following this, the epidural catheter will be inserted in the l2-l3 space once the epidural space is identified. Then the spinal injection will be given in the l3-l4 space using a spinal needle. You and I cannot decide which group you can belong to as it is randomized procedure.

SIDE EFFECTS: There are rare chances of the block leading to side effects like hypotension, vascular injection, epidural injection, epidural hematoma and nerve trauma.

BENEFITS: The most important benefit is excellent hemodynamic stability intra operatively. It will also help us get an idea about the adequacy of anesthesia and duration of anesthesia provided by isobaric bupivacaine.

REIMBURSEMENTS: You will not be charged for the drugs used in the study. In case of any o make sure anesthetic procedure related problems the department will bear the expenses.

CONFIDENTIALITY: Your identity will not be revealed at any stage of the study, either data analysis or final data for publishing. Only your study number will be used.

SHARING OF RESULT: The results I obtain from this study belong to Christian medical college and I am entitled to publish it in a journal or present in a conference. This

proposal has been reviewed and approved by the institutional review board (IRB) of CMC, which is a committee, whose task is that research participants are protected from harm. It has also been reviewed by the ethics committee of CMC Vellore, which is supporting the study.

RIGHT TO REFUSE OR WITHDRAW: You do not have to take part in this research if you do not wish to do so. You may also withdraw participating in the research even inside the operating room. It is your choice and all of your rights will be respected

CONTACT: Dr. Juliana Josphine. J, pg registrar, dept of anesthesia, CMCH, Vellore.632004

PART II

Informed consent

I---------- ----------

declare that I have read the information sheet provided to me / has been read to me, regarding this study and that I have clarified any doubts that I had. I also understand that my participation in this study is entirely voluntary and that I am free to withdraw from the study at any time without affecting my usual treatment or legal rights. I also understand that apart from the cost for the procedure, no extra expenditure will be incurred as part of the trial and that I will receive free treatment for any study related adverse event but will not receive any other financial compensation. I understand that the study staff and institutional ethics committee members will not need my permission to look at my health records. I agree to this access. I understand that my identity will not be revealed in any information released to third parties or published. I voluntarily agree to take part in this study

Name: Area for thumb impression:

Signature:

Date:

Name of witness:

Relation to participant:

Date:

Abstract:

A RANDOMISED CONTROL STUDY COMPARING THE EFFICACY OF 0.25% ISOBARIC BUPIVACAINE TO 0.5% HYPERBARIC BUPIVACAINE DURING SPINAL ANESTHESIA FOR HIP SURGERIES IN PEOPLE AGED 60 YEARS AND ABOVE.

Name of the department: Anesthesiology

Name of the candidate : JULIANA JOSPHINE.J

Name of the guide : Dr. SARAH NINAN

Degree and subject : MD Anesthesiology

Keywords – spinal anesthesia, hyperbaric Bupivacaine, isobaric Bupivacaine, hemodynamic stability.

Introduction:

The incidence of accidental falls seems to increase with an increase in age. This results in people of the elderly age group landing up with serious injuries like long bone fractures that require surgical intervention. Providing anesthesia to this age group can prove to be quite a challenge as a senior citizen usually presents with a number of co morbidities like hypertension, diabetes, ischemic heart disease and so on. Though regional anesthesia is advantageous in them, it becomes crucial for the anesthetist to maintain the hemodynamics intraoperatively. The chances of spinal hypotension can probably be lowered by reducing the baricity of the local anesthetic agent. Hence our goal was to see

if isobaric bupivacaine provided a more stable intra operative period compared to hyperbaric bupivacaine and we also compared the adequacy of sensory and motor blockade provided by them during surgery.

Methods:

After getting the approval of the institutional review board and estimating the sample size using Van Gessel's study, 31 patients were randomly allocated to two different groups by a computer generated sequence. The control group received 3ml (15mg) of 0.5% hyperbaric bupivacaine and the study group received 6ml (15mg) of 0.25% isobaric bupivacaine without any additives. All patients received the spinal anesthesia in the sitting position and were made supine almost immediately. Their blood pressure, heart rate and level of sensory and motor blockade were monitored intraoperatively and in the recovery room.

Results:

The incidence of hypotension and the need for ionotropic support was much lesser with 0.25% isobaric bupivacaine and it was statistically significant with a p value of 0.002 and 0.005 respectively. The time of onset, maximal cephalad spread and adequacy of motor and sensory blockade were similar with both groups. The overall complication rate was also much higher with the hyperbaric group with a significant p value of 0.001.

Conclusion:

0.25% isobaric bupivacaine provides a stable intraoperative hemodynamic condition compared to hyperbaric bupivacaine in the elderly population.

November 30, 2013

Dr. Juliana Josphine. J
PG Registrar
Department of Anesthesiology
Christian Medical College, Vellore 632 002

Sub: **Fluid Research grant project:**
Comparative study of spinal anesthesia with hyperbaric Bupivacaine versus isobaric Bupivacaine in people aged 60 years and above, posted for hip surgeries.
Dr. Juliana Josphine. J, PG Registrar, Anesthesiology, Dr. Sarah Ninan, Dr. Jeslin, Anesthesiology.

Ref: IRB Min. No. 8423 [INTERVEN] dated 21.08.2013

Dear Dr. Juliana Josphine. J,

The Institutional Review Board (Silver, Research and Ethics Committee) of the Christian Medical College, Vellore, reviewed and discussed your project titled "Comparative study of spinal anesthesia with hyperbaric Bupivacaine versus isobaric Bupivacaine in people aged 60 years and above, posted for hip surgeries." on August 21, 2013.

The committee reviewed the following documents:

1. Format for IRB application
2. Patient information Sheet and Informed Consent Form (English, Tamil, Telugu)
3. Curriculum Vitae' of Drs. Juliana Josphine. J, Sarah Ninan and Jeslin.
4. A CD containing document 1 – 3

Ethics Committee Silver, Office of Research, 1st Floor, Carman Block, Christian Medical College, Vellore, Tamil Nadu 632 002.
Tel : 0416 - 2284294, 2284202 Fax : 0416 - 2262788, 2284481 E-mail : research@cmcvellore.ac.in

Dr. George Thomas, D Ortho., Ph.D.,
Chairperson, Ethics Committee

Dr. B. Antonisamy, M.Sc., Ph.D., FSMS, FRSS.,
Secretary, Research Committee

Prof. Keith Gomez, B.Sc., M.A (S.W), M.Phil.,
Deputy Chairperson, Ethics Committee

Dr. Alfred Job Daniel, D Ortho, MS Ortho, DNB Ortho
Chairperson, Research Committee & Principal

Dr. Nihal Thomas,
MD., MNAMS., DNB (Endo), FRACP (Endo), FRCP (Glas) (EDIN)
Deputy Chairperson
Secretary, Ethics Committee, IRB
Additional Vice Principal (Research)

The following Institutional Review Board (Research & Ethics Committee) members were present at the meeting held on August 21, 2013 at 9.45 am in the CREST/SACN Conference Room, Christian Medical College, Bagayam, Vellore 632002.

Name	Qualification	Designation	Other Affiliations
Dr. Poonkuzhali	MSC, PhD	Professor, Haematology, CMC	Internal, Basic Medical Scientist
Dr. Binu Susan Mathew	MBBS, MD	Associate Professor, Dept. of Clinical Pharmacology	Internal, Pharmacologist
Dr. Suresh Devasahayam	BE, MS, PhD	Professor, Bioengineering, CMC	Internal, Basic Medical Scientist
Mrs. Pattabiraman	B Sc, DSSA	Social Worker, Vellore	External, Lay person
Mr. Sampath	B Sc, BL	Advocate	External, Legal Expert
Mr. Samuel Abraham	MA, PGDBA, PGDPM, M. Phil, BL.	Legal Advisor, CMC.	Internal, Legal Expert
Mrs. Mary Johnson	M.Sc	Professor, Child Health Nursing, CMC.	Internal, Nurse
Dr. Asha Mary Abraham	MBBS, MD, PhD	Professor, Virology, CMC	Internal, Clinician
Mrs. Selva Titus Chacko	M Sc	Professor, Medical Surgical Nursing, CMC	Internal, Nurse
Rev. Dr. Arul Dhas	M Sc, BD, DPC, PhD(Edin)	Chaplain, CMC	Internal, Social Scientist
Prof. Keith Gomez	BSc, MA (S.W), M. Phil (Psychiatry Social Work)	Deputy Chairperson (IRB) & Students' Counsellor, Loyola College, Chennai	External, Lay Person & Social Scientist
Dr. Jayaprakash Muliyil	BSC, MBBS, MD, MPH, DrPH(Epid), DMHC	Retired Professor, Vellore	External, Clinician & Epidemiologist

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Dr. B. Antonisamy	M Sc, PhD, FSMS, FRSS	Professor & Head Dept. of Biostatistics & Secretary IRB (RC), CMC	Internal, Statistician
Dr. Molly Jacob	MBBS, MD, PhD	Professor, Biochemistry, CMC	Internal, Clinician
Dr. Prathap Tharyan	MD, MRC Psych.	Professor of Psychiatry, CMC	Internal, Clinician
Dr. P. Zachariah	MBBS, PhD	Retired Professor, Vellore.	External, Scientist
Dr. Nihal Thomas	MD MNAMS DNB(Endo) FRACP (Endo) FRCP(Edin) FRCP (Glasg)	Secretary IRB (EC)& Dy. Chairperson (IRB), Professor of Endocrinology & Addl. Vice Principal (Research), CMC.	Internal, Clinician

We approve the project to be conducted as presented.

The Institutional Ethics Committee expects to be informed about the progress of the project, any **adverse events** occurring in the course of the project, any **amendments in the protocol and the patient information / informed consent**. On completion of the study you are expected to submit a copy of the **final report**. A detailed presentation of your data will have to be reported at the Data Safety Monitoring Board. Respective forms can be downloaded from the following link: http://172.16.11.136/Research/IRB Polices.html in the CMC Intranet and in the CMC website link address: http://www.cmch-vellore.edu/static/research/Index.html.

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November 30, 2013

Dr. Juliana Josphine. J
PG Registrar
Department of Anesthesiology
Christian Medical College, Vellore 632 002

Sub: **Fluid Research grant project:**
Comparative study of spinal anesthesia with hyperbaric Bupivacaine versus isobaric Bupivacaine in people aged 60 years and above, posted for hip surgeries.
Dr. Juliana Josphine. J, PG Registrar, Anesthesiology, Dr. Sarah Ninan, Dr. Jeslin, Anesthesiology.

Ref: IRB Min. No. 8423 [INTERVEN] dated 21.08.2013

Dear Dr. Juliana Josphine. J,

I enclose the following documents:-

1. Institutional Review Board approval
2. Agreement

Could you please sign the agreement and send it to Dr. Nihal Thomas, Addl. Vice Principal (Research), so that the grant money can be released.

With best wishes,

Dr. Nihal Thomas
Secretary (Ethics Committee)
Institutional Review Board

Dr. NIHAL THOMAS
MD.,MNAMS.,DNB(Endo),FRACP(Endo),FRCP(Edin),FRCP(Glasg)
SECRETARY - (ETHICS COMMITTEE)
Institutional Review Board,
Christian Medical College, Vellore - 632 002.

Ethics Committee Silver, Office of Research, 1st Floor, Carman Block, Christian Medical College, Vellore, Tamil Nadu 632 002.
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ID	AGE	HT	ASA	PROCE	DIAG	DRUG	BSSBP	BSDBP	BSMAP	BSHR	TIME	ONSET	SENLV	MOTOR	EPIDU	TIME1	DURA	RSBP
1	60	154	111	DHS	NOF FRACTURE	1	130	80	96	84	11.30	2.00	T6	1	N	3.10	3.40	116
2	81	160	11	DHS	IT FRACTURE	2	137	68	91	108	12.15	3.00	T5	1	N	2.05	1.30	109
3	68	170	11	DHS	IT FRACTURE	2	147	67	93	96	7.45	3.00	T6	1	N	11.40	3.50	166
4	64	160	11	HIP PFN	SUBT FRACTURE	1	132	75	96	96	3.35	4.00	T12	1	Y	7.30	3.50	110
5	62	158	111	HEMIARTHROPLASTY	NOF FRACTURE	2	122	74	86	91	8.00	1.10	T5	1	N	9.15	1.20	113
6	75	170	1	DHS	IT FRACTURE	1	110	76	87	86	4.10	3.00	T7	1	N	8.15	5.00	169
7	86	166	11	DHS	NOF FRACTURE	1	144	78	100	86	7.40	2.40	T6	1	N	11.20	3.40	113
8	75	168	11	DHS	NOF FRACTURE	1	150	80	103	108	8.22	2.25	T6	1	N	11.45	3.20	120
9	78	172	11	HEMIARTHROPLASTY	NOF FRACTURE	2	138	79	92	83	11.15	5.00	T8	1	N	1.25	2.00	140
10	75	163	11	HEMIARTHROPLASTY	NOF FRACTURE	2	144	69	89	67	7.50	2.05	T10	1	N	10.20	2.25	129
11	75	166	11	DHS	IT FRACTURE	2	164	69	90	93	5.20	3.20	T6	1	Y	9.10	4.00	136
12	66	168	11	DHS	NOF FRACTURE	2	130	66	87	90	2.34	2.10	T6	1	N	4.20	1.50	129
13	85	167	11	PFN	IT FRACTURE	1	154	52	86	56	8.00	3.10	T5	1	Y	11.17	3.20	97
14	73	154	1	DHS	IT FRACTURE	1	143	70	94	100	8.00	5.00	T5	1	N	10.25	2.20	135
15	70	176	1	DHS	IT FRACTURE	1	146	78	100	105	6.35	5.00	T8	1	N	8.20	1.40	147
16	65	160	1	DHS	IT FRACTURE	1	111	73	85	89	11.30	2.30	T8	1	Y	3.00	3.30	134
17	70	162	11	DHS	IT FRACTURE	2	184	90	121	85	12.30	2.00	T6	1	Y	5.25	4.55	158
18	60	160	1	DHS	IT FRACTURE	2	131	85	100	108	11.20	2.20	T7	1	N	2.00	2.40	143
19	80	155	11	DHS	IT FRACTURE	1	136	71	86	106	2.00	5.00	T6	1	N	5.00	3.00	110
20	74	165	11	DHS	IT FRACTURE	1	162	82	101	94	9.30	5.00	T7	1	Y	1.00	3.40	138
21	73	163	11	DHS	IT FRACTURE	2	133	77	92	131	12.00	4.00	T6	1	N	2.15	2.10	129
22	65	174	11	DHS	IT FRACTURE	2	137	79	98	69	7.56	1.50	T7	1	N	10.20	2.10	145
23	80	167	1	DHS	IT FRACTURE	1	147	83	104	99	7.45	2.20	T4	1	N	11.10	3.40	140
24	60	155	1	DHS	IT FRACTURE	2	150	83	107	88	3.35	3.00	T6	1	N	5.00	1.30	140
25	86	155	11	DHS	IT FRACTURE	1	179	85	107	97	3.40	4.00	T5	1	N	6.00	2.20	126
26	78	161	11	DHS	IT FRACTURE	2	163	87	106	99	8.52	3.00	T7	1	N	11.20	2.10	121
27	72	166	1	DHS	IT FRACTURE	2	125	76	88	77	1.41	4.40	T7	1	N	3.30	2.45	118
28	78	168	11	HEMIARTHROPLASTY	NOF FRACTURE	1	170	95	114	110	11.45	3.00	T9	1	N	2.30	2.45	135
29	81	169	11	PFN	IT FRACTURE	2	150	83	100	87	1.55	3.00	T10	1	Y	5.00	3.05	113
30	60	162	11	DHS	IT FRACTURE	1	113	75	84	84	10.00	5.05	T6	1	N	1.55	3.50	130
31	79	170	1	DHS	NOF FRACTURE	1	140	71	88	100	8.10	2.10	T6	1	Y	10.20	2.20	120

ID	RDBP	RMAP	RHR	RSENLV	RMOTLV	COMPLI	COMM	REQVS	S1	S2	S3	S4
1	79	87	87	T10	2	NIL	NIL	300UG PNP	105	141	88	137
2	48	68	86	T10	2	NIL	NIL	100UG PNP	120	111	106	108
3	70	102	120	T11	3	NIL	NIL	400UG PNP	118	142	141	152
4	86	93	104	T8	2	HYPOTENSION	RETURN OF MOTOR POWER EPIDURAL ACTIVATED	900UG PNP NOR ADR	116	126	100	90
5	71	82	97	T6	1	NIL	NIL	NIL	99	90	109	113
6	90	105	92	L2	4	HYPOTENSION	CONVERTED TO GA AS PT RESTLESS	100UG PNP NOR ADR	108	103	104	102
7	55	65	88	T10	1	HYPOTENSION	NIL	900UG PNP NOR ADR	126	116	99	89
8	70	64	120	T10	4	NIL	NIL	800UG PNP	118	96	102	116
9	80	98	100	T10	2	NIL	NIL	NIL	131	103	98	113
10	76	85	77	T12	3	NIL	NIL	NIL	144	149	114	126
11	68	90	107	T10	6	NIL	RETURN OF MOTOR POWER EPIDURAL ACTIVATED	50 PNP 5 EPI	97	92	120	147
12	73	91	81	T12	1	HYPOTENSION	NIL	300UG PNP NOR ADR	124	86	73	105
13	36	56	50	T12	3	HYPOTENSION	PAIN EPIDURAL ACTIVATED	1800UG PNP 100MG EPI	142	117	84	101
14	85	101	117	T8	1	HYPOTENSION	NIL	700UG PNP NOR ADR	114	120	77	72
15	80	101	81	L2	2	NIL	NIL	NIL	157	141	129	119
16	67	89	96	T12	3	HYPOTENSION	RETURN OF MOTOR POWER EPIDURAL ACTIVATED	NOR ADR	126	97	167	125
17	81	107	80	L1	3	NIL	PAIN EPIDURAL ACTIVATED	EPI 10MG	155	117	106	104
18	70	94	108	T12	2	NIL	NIL	700UG PNP	104	121	94	84
19	66	77	115	T10	2	HYPOTENSION	NIL	PNP 200UG NOR ADR	117	105	117	82
20	78	94	75	T10	3	NIL	PAIN EPIDURAL ACTIVATED	NIL	127	129	125	112
21	68	82	138	L2	5	NIL	NIL	PNP 200UG	92	91	108	118
22	75	98	80	T12	2	NIL	NIL	EPI 20MG	103	96	79	93
23	71	98	97	L2	6	HYPOTENSION	NIL	NOR ADR PNP 200UG	147	126	124	132
24	58	85	78	L2	3	NIL	NIL	PNP 400UG EPI 10MG	99	97	99	104
25	62	74	81	T11	2	HYPOTENSION	NIL	NOR ADR PNP 300UG	115	82	119	93
26	68	79	112	T10	4	NIL	NIL	PNP 700UG EPI 5MG	114	118	99	101
27	66	72	76	T12	2	NIL	NIL	PNP 900UG EPI 5MG	100	93	100	78
28	79	94	92	T10	6	HYPOTENSION	NIL	NOR ADR PNP 200UG	137	136	122	105
29	67	78	100	T11	3	HYPOTENSION	PAIN EPIDURAL ACTIVATED	NOR ADR PNP700UG EPI	138	111	83	91
30	96	102	96	L1	6	HYPOTENSION	NIL	NOR ADR PNP 200UG	124	81	73	71
31	66	84	97	T12	2	NIL	PAIN EPIDURAL ACTIVATED	650UG PNP 20MG EPI	140	50	111	105

ID	S5	S6	S7	S8	S9	S10	S11	S12	S13	S14	S15	S16	S17	S18	S19	S20	S21	S22	S23	S24	D1	D2	D3	D4	D5	D6	D7	D8	D9
1	127	92	109	111	116	105	106	112	110	112	106	102	113	117	115	112	114	115	114	115	66	74	56	74	71	60	58	64	58
2	112	110	108	109	106	101	100	109	107	109	111	114	112	118	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	52	48	51	48	49	48	49	50	52
3	121	104	120	102	121	108	107	122	106	99	133	96	138	128	130	127	108	112	111	110	69	82	94	60	48	69	60	70	68
4	92	105	85	90	100	87	97	108	106	113	107	116	118	114	101	97	112	120	118	120	69	72	63	48	48	28	42	48	56
5	105	102	90	98	96	102	104	102	110	117	112	108	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	69	65	77	83	76	72	65	68	70
6	101	108	100	118	117	118	111	117	122	120	118	117	122	117	124	128	130	138	140	90	68	64	63	63	64	69	65	69	69
7	107	92	93	100	88	89	103	94	89	111	94	89	100	91	83	87	83	151	106	103	60	62	52	48	56	50	57	52	52
8	104	100	112	114	118	112	118	120	111	131	131	120	131	128	128	130	134	133	131	130	54	56	60	72	72	66	62	52	50
9	118	115	113	106	108	111	108	105	106	111	119	120	126	142	140	139	148	147	148	148	71	71	70	77	75	79	72	73	75
10	117	116	107	124	117	117	142	127	112	139	133	110	114	109	115	117	118	120	122	120	86	89	69	77	68	67	65	75	74
11	147	133	133	145	145	147	147	154	148	156	146	119	128	120	129	131	140	143	131	142	36	46	41	59	61	60	68	58	55
12	102	100	92	103	83	110	107	108	113	107	121	130	127	144	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	64	47	45	58	61	63	55	55	45	56
13	123	114	103	98	124	100	86	130	113	127	110	120	104	112	105	115	102	112	111	115	51	45	34	40	38	40	42	39	83
14	93	92	134	78	82	87	90	88	107	104	97	83	114	121	136	148	154	148	148	148	43	100	55	34	53	75	87	38	47
15	115	127	128	125	125	112	127	129	131	152	143	146	147	148	161	147	#NULL!	#NULL!	#NULL!	#NULL!	84	77	65	60	55	50	57	54	56
16	107	97	132	115	112	154	124	103	112	120	105	121	99	118	128	127	126	118	114	110	63	71	76	57	53	48	61	56	49
17	134	121	120	127	100	106	130	112	116	120	130	135	136	121	120	117	#NULL!	#NULL!	#NULL!	#NULL!	62	50	47	47	54	57	56	54	64
18	90	93	104	82	80	100	100	101	104	139	78	91	102	96	104	91	102	103	104	115	91	85	67	49	61	61	69	55	53
19	104	103	100	103	109	106	103	100	105	106	110	111	108	110	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	60	57	64	46	50	49	50	47	51
20	105	115	119	121	123	125	122	127	147	142	137	133	131	129	136	140	139	141	150	159	70	73	89	62	61	60	68	70	69
21	108	101	97	116	107	112	125	125	127	126	122	121	125	126	125	129	130	128	126	128	56	56	54	58	52	37	65	50	42
22	90	93	102	99	107	108	100	97	97	103	102	101	110	123	120	113	127	130	140	148	79	62	46	43	47	46	49	50	51
23	130	129	119	112	89	111	94	110	132	108	123	106	116	93	109	99	141	102	112	112	83	81	76	87	95	80	81	60	41
24	80	83	88	99	88	84	108	90	111	119	120	117	115	120	121	139	140	150	144	156	49	53	55	52	37	33	41	43	37
25	134	150	152	71	140	154	132	138	111	150	104	135	90	110	120	134	128	142	128	142	80	48	63	44	89	126	88	32	88
26	92	119	110	81	94	123	117	112	105	114	110	114	117	120	120	108	119	99	124	130	79	60	56	47	64	62	58	50	50
27	146	79	110	78	133	120	104	114	83	117	95	113	90	97	93	98	85	126	108	105	69	58	29	34	128	54	56	36	64
28	98	107	120	111	103	113	139	132	133	134	130	107	115	117	121	117	117	129	126	129	80	72	57	50	54	47	56	70	75
29	134	106	123	154	110	137	172	99	98	109	116	120	119	149	134	141	151	141	139	141	73	89	61	61	53	61	82	54	49
30	80	117	79	116	115	118	121	108	111	105	115	111	95	102	102	103	104	110	103	111	91	35	35	34	54	47	55	62	62
31	102	92	104	122	120	123	120	149	153	144	156	135	91	98	95	93	106	84	101	101	64	27	71	67	58	55	73	75	76

ID	D10	D11	D12	D13	D14	D15	D16	D17	D18	D19	D20	D21	D22	D23	D24	M1	M2	M3	M4	M5	M6	M7	M8	M9	M10	M11	M12
1	58	54	60	60	56	58	62	60	59	64	64	62	66	62	64	77	84	63	88	85	68	70	76	72	69	70	72
2	54	56	60	62	61	57	59	60	61	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	78	69	69	68	68	68	70	74	70	70	71	76
3	88	58	59	66	62	60	80	88	68	69	90	82	76	74	74	85	102	109	90	72	80	80	80	85	94	75	80
4	58	58	57	59	55	62	51	60	56	55	47	59	61	66	68	84	90	75	62	62	54	56	62	70	68	74	74
5	70	68	70	64	93	92	88	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	76	70	85	90	81	76	71	74	78	78	76	78
6	68	69	69	68	69	70	70	80	83	84	86	88	90	91	60	81	77	76	76	76	82	76	85	85	85	83	85
7	50	54	49	52	62	54	55	50	56	57	51	51	93	55	56	76	62	63	59	67	61	66	61	60	60	64	58
8	52	76	86	72	88	87	62	70	76	74	76	84	80	82	82	75	69	74	86	82	74	78	72	72	72	90	97
9	79	79	69	71	74	83	82	79	85	78	88	82	83	84	84	86	79	76	86	85	87	82	81	83	86	84	78
10	74	91	80	73	87	83	73	75	70	74	76	78	80	81	81	67	66	65	63	67	65	63	62	59	62	61	63
11	59	61	64	63	68	54	63	56	66	57	57	49	55	58	56	52	55	60	81	81	78	77	77	75	82	85	85
12	54	60	59	57	61	69	92	57	60	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	84	60	54	74	74	75	67	71	57	74	72	76
13	51	42	57	43	39	52	38	39	52	50	51	49	44	57	57	75	63	48	57	57	57	55	55	61	64	49	73
14	43	44	46	48	43	45	48	51	54	72	75	78	75	78	78	60	108	59	43	63	79	100	42	54	46	60	61
15	52	55	57	56	68	61	67	72	72	83	78	#NULL!	#NULL!	#NULL!	#NULL!	103	91	80	75	68	66	72	72	74	68	73	73
16	66	58	48	56	52	68	68	74	60	56	57	56	61	50	55	80	77	96	73	66	60	78	71	64	88	73	61
17	52	60	67	50	55	66	67	66	67	68	68	#NULL!	#NULL!	#NULL!	#NULL!	93	72	67	66	80	78	77	75	75	76	70	83
18	57	57	56	80	52	59	54	72	59	69	54	72	69	70	75	94	94	72	57	68	65	77	62	59	59	63	64
19	51	50	48	50	51	54	56	55	56	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	71	64	78	52	60	59	60	60	63	62	62	60
20	70	71	79	80	70	74	66	74	74	75	76	76	79	77	76	83	86	98	74	71	77	79	82	82	83	84	84
21	41	39	37	40	42	44	45	46	50	51	55	54	55	52	53	63	63	68	73	65	54	73	64	60	59	69	59
22	58	50	54	46	47	57	57	52	55	54	59	67	80	73	75	98	76	62	55	62	60	63	67	67	74	69	69
23	41	35	53	54	57	49	60	55	36	49	39	52	40	48	52	97	92	88	99	101	92	89	72	50	58	44	68
24	42	45	51	48	56	59	62	46	48	59	48	47	66	71	70	60	62	65	62	49	45	53	57	50	52	62	61
25	71	59	55	44	58	53	52	52	64	64	84	84	72	64	64	89	56	75	56	99	132	110	40	96	89	76	73
26	62	63	60	64	63	65	62	59	71	52	62	69	55	66	75	87	74	67	59	71	75	71	57	61	76	75	72
27	106	62	76	53	60	55	51	56	57	60	64	54	69	62	58	77	66	45	43	133	59	69	46	81	109	72	86
28	66	71	82	80	74	74	70	60	62	62	66	67	65	66	66	94	84	71	63	61	57	67	82	86	75	79	96
29	57	72	46	44	48	43	43	43	54	48	51	50	53	55	61	89	94	67	68	73	72	91	79	62	75	97	59
30	54	63	54	65	73	59	60	62	62	64	76	70	63	62	67	99	45	44	42	60	70	51	70	75	76	69	73
31	70	75	79	88	82	75	61	56	55	57	65	55	55	54	76	82	30	80	77	66	65	81	86	88	84	87	97

ID	M13	M14	M15	M16	M17	M18	M19	M20	M21	M22	M23	M24	HR1	HR2	HR3	HR4	HR5	HR6	HR7	HR8	HR9	HR10	HR11	HR12	ID
1	71	69	70	68	74	75	77	74	72	79	76	75	104	73	77	75	85	68	70	76	72	59	61	64	1
2	75	76	72	73	75	76	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	102	96	94	93	93	90	91	90	87	86	84	84	2
3	79	74	84	85	104	88	89	102	90	88	86	86	96	97	98	99	90	96	98	86	80	68	84	78	3
4	78	74	77	72	79	75	70	63	76	81	83	85	93	92	96	82	69	72	66	67	65	70	69	73	4
5	78	96	94	92	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	93	96	91	96	90	88	97	96	92	90	88	87	5
6	86	86	89	89	94	94	97	100	102	106	107	80	84	86	83	82	82	83	88	82	81	80	80	86	6
7	62	74	63	63	59	66	67	59	57	109	67	68	82	82	84	84	88	86	88	90	91	90	86	88	7
8	85	102	101	81	90	93	92	94	104	97	98	98	108	107	107	106	104	102	102	101	100	100	102	106	8
9	78	82	91	89	88	97	93	100	96	96	98	98	84	86	88	84	82	83	81	80	77	76	76	73	9
10	72	70	73	74	73	72	74	76	78	80	81	81	67	66	65	63	67	65	63	62	59	62	61	63	10
11	83	86	76	78	75	74	75	76	73	77	78	76	93	90	94	90	89	89	88	87	87	84	84	82	11
12	77	73	81	89	103	86	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	92	90	85	80	76	73	71	70	69	69	70	70	12
13	61	61	65	58	60	65	61	66	59	60	68	66	58	56	51	51	54	55	54	55	54	55	61	64	13
14	63	60	57	61	67	70	84	95	100	95	96	96	100	104	107	99	98	96	100	103	108	100	98	96	14
15	73	82	79	87	87	88	99	95	#NULL!	#NULL!	#NULL!	#NULL!	86	92	95	89	84	77	96	79	79	79	78	78	15
16	71	67	75	78	80	75	74	76	76	75	65	68	88	86	78	80	81	88	82	83	80	78	74	70	16
17	82	72	76	87	89	89	85	85	#NULL!	#NULL!	#NULL!	#NULL!	80	75	70	66	66	76	72	70	70	62	74	74	17
18	86	71	64	63	75	68	76	63	75	76	76	84	104	102	96	99	84	80	89	89	85	84	81	77	18
19	59	60	64	63	64	65	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	104	103	101	96	90	98	100	101	98	98	99	100	19
20	96	88	88	83	86	85	73	72	71	71	71	73	88	86	90	84	81	80	79	70	70	70	79	79	20
21	60	63	64	63	66	64	63	65	66	68	67	66	128	126	100	100	100	108	109	110	120	117	117	120	21
22	63	63	72	68	70	72	80	84	83	94	100	99	69	67	73	69	69	68	69	73	73	74	73	72	22
23	72	69	68	70	69	51	63	53	74	55	65	66	96	95	90	88	89	88	86	86	80	78	80	74	23
24	65	72	70	75	65	67	72	72	69	82	87	92	83	84	73	67	69	65	55	62	64	64	65	71	24
25	57	77	59	68	61	72	76	90	86	85	76	74	93	90	86	88	88	87	86	81	80	70	84	84	25
26	74	73	77	75	74	78	68	73	81	65	82	88	109	108	109	95	78	76	82	80	80	94	95	95	26
27	61	73	64	65	64	67	68	72	62	83	72	70	80	77	80	60	57	71	63	75	75	73	86	77	27
28	91	87	87	83	71	74	74	78	79	78	79	79	110	91	87	90	92	88	86	88	87	90	90	88	28
29	55	61	62	62	62	77	70	72	75	74	76	80	77	84	69	66	65	72	68	69	72	72	70	68	29
30	68	74	84	73	69	72	72	73	83	79	74	75	80	88	84	86	72	72	72	72	65	64	73	75	30
31	105	97	98	80	65	65	66	72	66	63	66	79	118	107	101	106	100	104	96	91	85	84	86	92	31

HR13	HR14	HR15	HR16	HR17	HR18	HR19	HR20	HR21	HR22	HR23	HR24
64	74	77	81	69	62	70	81	90	60	66	74
83	84	76	78	82	86	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!
90	94	96	106	108	112	102	110	106	112	110	111
74	73	73	74	80	82	83	76	78	86	87	93
87	90	93	92	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!
84	83	83	83	82	82	80	81	84	84	86	90
87	85	83	84	88	86	87	87	88	88	87	#NULL!
101	98	98	97	106	110	110	110	110	112	111	111
72	70	70	72	72	74	75	80	84	88	90	96
72	70	73	74	73	72	74	76	78	80	81	81
80	78	77	76	74	77	80	81	77	76	78	79
74	76	76	76	77	78	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!
67	65	66	72	70	70	69	67	70	73	73	73
91	96	90	94	90	90	89	88	88	84	86	90
78	78	81	81	82	79	83	81	#NULL!	#NULL!	#NULL!	#NULL!
71	67	66	68	67	65	63	64	68	67	68	69
82	86	88	92	90	94	88	86	#NULL!	#NULL!	#NULL!	#NULL!
74	83	79	79	79	78	76	70	74	73	78	75
104	105	107	108	107	110	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!
79	80	77	75	75	74	71	73	72	71	71	73
121	120	121	122	119	122	118	117	116	117	120	122
72	70	70	71	71	73	75	74	75	75	74	74
78	77	80	81	82	76	78	80	85	86	88	84
73	75	76	72	72	71	64	68	70	65	66	66
66	63	65	62	61	69	58	61	72	80	81	79
95	98	99	101	101	102	102	103	102	103	94	99
66	67	60	61	62	61	62	60	63	59	60	62
87	88	88	90	91	90	88	90	91	91	91	92
70	67	64	66	69	72	67	65	70	70	72	74
74	72	70	76	67	74	64	71	73	72	71	71
95	91	93	96	103	99	104	103	103	103	102	103