Continuous Femoral Versus Epidural for Analgesia in the management of Knee Surgery

submitted for fulfillment for M.D degree in anesthesia and ICU

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<td>Acetyl choline</td>
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<td>ACL</td>
<td>Anterior crural ligament</td>
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<td>ANOVA</td>
<td>Analysis of variance</td>
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<td>BP</td>
<td>Blood Pressure</td>
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<td>CFNB</td>
<td>Continuous femoral nerve block</td>
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<td>CT</td>
<td>Computed tomography</td>
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<td>Electromyography</td>
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<td>FNB</td>
<td>Femoral nerve block</td>
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<td>GABA</td>
<td>Gama amino buteric acid</td>
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<td>HR</td>
<td>Heart rate</td>
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<td>LD50</td>
<td>Lethal dose 50</td>
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<td>mA</td>
<td>Mille ampere</td>
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<td>MAC</td>
<td>Minimum alveolar concentration</td>
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<td>MRI</td>
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<td>MS</td>
<td>Mobilization score</td>
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<td>NMDA</td>
<td>N-methyl-D-aspartate receptors</td>
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<td>NRS-R</td>
<td>Numeric rating scale at rest</td>
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<td>NRS-M</td>
<td>Numeric rating scale with movement</td>
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<td>PABA</td>
<td>P-amino benzoic acid</td>
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<td>PACU</td>
<td>Post anesthesia care unit</td>
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<td>Patient controlled analgesia</td>
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<td>Peripheral nerve stimulator</td>
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<td>t1/2</td>
<td>Half-life</td>
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<td>VAS</td>
<td>Visual analogue scale</td>
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AHMED MOSTAFA IBRAHIM ABO SAKAYA
Introduction

Regional anesthesia at the lower limb has been demonstrated to be a valuable technique for the management of immediate postoperative pain after orthopedic surgery. In addition, postoperative continuous femoral block has been shown to hasten recovery and rehabilitation processes and therefore decrease the length of hospital stay of knee surgery patients. Continuous lower extremity blocks provide superior analgesia with fewer side effects, improve perioperative outcomes, and accelerate hospital dismissal after major joint replacement. (Motamed, et al.,2009)

Postoperative pain is mainly caused by tissue inflammation. Mediators of inflammation include bradykinin, serotonin, prostaglandins, histamine, leukotrienes, and cytokines. Cytokines are important mediators of local and systemic inflammatory response after surgery. In addition, cytokines are involved in nociception and development of hyperalgesia. Several animal experiments show that pre-incisional blockade may limit the development of peripheral inflammation in the corresponding innervated zone. In addition, lidocaine and bupivacaine seem to have a systemic antiinflammatory effect, and bupivacaine can reduce cytokine production through a local and systemic effect. (Martin, et al.,2008)

The femoral nerve is formed within the psoas major muscle by posterior divisions of the second, third, and fourth lumbar nerves. It emerges from the lateral border of the psoas muscle, descends in the groove between the psoas and iliacus muscles, and enters the thigh by passing beneath the inguinal ligament lateral to the femoral artery. At this point the nerve divides into multiple terminal branches, which have been classified as anterior and posterior. The anterior branches are primarily cutaneous, and the deep branches are chiefly motor. The femoral nerve
supplies the anterior compartment muscles of the thigh (i.e., quadriceps, sartorius) and the skin of the anterior aspect of the thigh from the inguinal ligament to the knee. Its terminal branch is the saphenous nerve, which supplies an area of skin along the medial side of the leg from the knee to the big toe. *(Marhofer et al., 2000)*

The perivascular approach (i.e., 3-in-1 block) to the lumbar plexus is based on the premise that injection of a large volume of local anesthetic within the femoral canal while maintaining distal pressure will result in proximal spread of solution into the psoas compartment and consequent lumbar plexus block. However, recent imaging studies suggest that blockade occurs through lateral (lateral femoral cutaneous nerve) and medial (obturator nerve) spread of injected solution. *(Marhofer et al., 2000)*

Intravascular injection and hematoma are possible because of the proximity of the femoral artery. Anatomically, the nerve and artery are located in separate sheaths approximately 1 cm apart. In most patients with normal anatomy, the femoral artery can easily be palpated to allow correct, safe needle positioning lateral to the pulsation. The presence of femoral vascular grafts is a relative contraindication to these techniques. Nerve damage is rare.*(Capdevila et al., 2005)*

Advantages cited for continuous nerve blockade include prolongation of surgical anesthesia, decreased risk for toxicity because of lower incremental doses, and postoperative pain relief and sympathectomy. Catheter placement using over-the-needle and through-the-needle methods have been described. Advances in equipment technology, including the development of stimulating needles and catheters and portable pumps allowing infusion of local anesthetic after hospital dismissal, have increased the success rate and popularity of continuous
peripheral blockade. Overall, continuous peripheral nerve blockade provides analgesia superior to that of conventional opioid therapy. Minor technical problems, such as catheter kinking, displacement, or leakage and bacterial colonization, are frequent, with no adverse clinical consequences in the large majority of cases. However, major neurologic and infectious adverse events are rare. (*Ilfeld et al., 2002*)

The choice of local anesthetic for a peripheral nerve block obviously depends to some degree on the duration of the surgical procedure, although other factors are also important. Prolonged blockade for up to 24 hours often occurs with long-acting agents such as bupivacaine or ropivacaine. Although such blockade results in good postoperative pain relief for an inpatient, it may be undesirable for an ambulatory patient because of the possible risk of nerve or tissue injury in a partially blocked limb. A short- or medium-acting agent, such as lidocaine or mepivacaine, may be more appropriate in the outpatient setting. Whatever drug is chosen, the total dosage should be calculated for each patient and be kept within acceptable safe limits. (*Ilfeld et al., 2002*)

The highest concentrations of local anesthetic drugs are not appropriate for peripheral neural blockade; therefore, 0.75% bupivacaine or ropivacaine, 2% lidocaine, 2% mepivacaine, and 3% 2-chloroprocaine are not recommended. Conversely, the lowest concentrations of the same agents (i.e., 0.25% bupivacaine or ropivacaine and 0.5% mepivacaine or lidocaine) may not provide complete motor blockade. (*Motamed et al., 2009*)

Analgesia delivered through an indwelling epidural catheter is a safe and effective method for management of acute postoperative pain. Postoperative epidural analgesia can provide analgesia superior to that with systemic opioids. Intraoperative use of the epidural catheter as part
of a combined epidural-general anesthetic technique results in less pain and faster patient recovery immediately after surgery than general anesthesia followed by systemic opioids does. Each of these options may affect the quality of postoperative analgesia, patient-reported outcomes, and even rates of morbidity and mortality. (Richman et al., 2005)

Clonidine is a frequently used adjuvant to local anesthetics (LA). The analgesic properties of clonidine when administered intrathecally or epidurally have been demonstrated; they seem to be attributable to its $\alpha_2$ agonist properties. The benefit of adding clonidine to LAs for peripheral nerve blocks is less clear, although it is widely believed that clonidine improves quality and duration of aLAblock. (Elia et al., 2008)

The choice of local anesthetic for continuous epidural infusion varies. In general, bupivacaine, ropivacaine, or levobupivacaine is chosen because of the differential and preferential clinical sensory blockade with minimal impairment of motor function. Concentrations used for postoperative epidural analgesia ($\leq 0.125\%$ bupivacaine or levobupivacaine or $\leq 0.2\%$ ropivacaine) are lower than those used for intraoperative anesthesia. (Curatolo et al., 2000)

A variety of adjuvants may be added to epidural infusions to enhance analgesia while minimizing side effects, but none has gained widespread acceptance. Two of the more studied adjuvants are clonidine and epinephrine. Clonidine mediates its analgesic effects primarily through the spinal dorsal horn $\alpha_2$-receptors on primary afferents and interneurons, as well as the descending noradrenergic pathway, and the epidural dose typically used ranges from 5 to 20 $\mu$g/hr. Clinical application of clonidine is limited by its side effects: hypotension, bradycardia, and sedation. Hypotension and bradycardia are both dose dependent. Epinephrine may improve epidural analgesia, can increase sensory blockade, and is
generally administered at a concentration of 2 to 5 $\mu$g/mL. Epidural administration of NMDA antagonists, such as ketamine, can theoretically be useful in attenuating central sensitization and potentiating the analgesic effect of epidural opioids, but additional safety and analgesic data are needed. (Sakaguchi et al., 2000)
**Aim of the Work**

This thesis is suggested to compare between continuous epidural and continuous femoral 3 in 1 block as postoperative analgesia in knee surgery.
Anatomy of The Epidural Space

Fig.(1): Ligamentum flavum and epidural space

The spinal cord has three covering membranes or meninges the dura mater, arachnoid mater and pia mater.

The dural covering of the brain is a double membrane, between the walls of which lie the cerebral venous sinuses. The dura mater that encloses the cord consists of a continuation of the inner (meningeal) layer of the cerebral dura, which is made up of dense fibrous tissue; the outer (endosteal) layer of the cerebral dura terminates at the foramen magnum, where it merges with the periosteum enclosing the skull, and is thereafter represented by the periosteal lining of the vertebral canal. The dural sac usually extends to the level of the 2nd segment of the sacrum; occasionally it ends as high as L5, at other times it extends to S3.
As a result of this, it is occasionally possible to perform an inadvertent spinal tap during the course of a caudal injection (Newell, 1999).

The dural sheath then continues as the covering of the filum terminale to end by adhering to the periosteum on the back of the coccyx. The sac widens out in both the cervical and lumbar regions, corresponding to the cervical and lumbar enlargements of the spinal cord. It lies rather loosely within the spinal canal, buffered in the epidural fat, but it is attached at the following points to its bony surroundings:

Above, to the edges of the foramen magnum and to the posterior aspects of the bodies of the 2nd and 3rd cervical vertebrae.

Anteriorly, by slender filaments of fibrous tissue to the posterior longitudinal ligament.

Laterally, by prolongations along the dorsal and ventral nerve roots, which fuse into a common sheath and which then blend with the epineurium of the resultant spinal nerves.

Inferiorly, by the filum terminale to the coccyx.

However, the dural sac is completely free posteriorly.

Fig. (2): Spinal cord, epidural space and ligamentum flavum
The arachnoid mater is a delicate membrane which lines the dural sheath and which sends prolongations along each nerve root. Above, it is continuous with the cerebral arachnoid, which loosely invests the brain, and which dips into the longitudinal fissure between the cerebral hemispheres.

The pia mater is the innermost of the three membranes, is a vascular connective tissue sheath that closely invests the brain and spinal cord, and projects into their sulci and fissures. The spinal pia is thickened anteriorly into the linea splendens along the length of the anterior median fissure.

On either side, it forms the ligamentum denticulatum, a series of triangular fibrous strands attached at their apices to the dural sheath; they are 21 in number, and lie between the spinal nerves down to the gap between the 12th thoracic and 1st lumbar root. The lowermost denticulation is bifid and is crossed by the 1st lumbar nerve root. (Ellis et al., 2004).

The posterior subarachnoid septum consists of an incomplete sheet of pia passing from the posterior median sulcus of the cord backwards to the dura in the midline. Inferiorly, the pia is continued downwards as the filum terminal, which pierces the lower end of the dural sac and then continues to the coccyx with a covering sheath of dura. The compartments related to the spinal meninges are the subarachnoid, subdural and epidural spaces.

The subarachnoid space contains the CSF. It is traversed by incomplete trabeculae the posterior subarachnoid septum and the ligamentum denticulatum, which have already been described. This space communicates with the tissue spaces around the vessels in the pia mater that accompany them as they penetrate into the cord. (Newell, 1999).
The subdural space is a potential one only; the arachnoid is in close contact with the dural sheath and is separated from it only by a thin film of serous fluid. The subdural space within the vertebral canal rarely enters the consciousness of the clinician, unless it is the accidental site of catheter placement during attempted epidural analgesia or anaesthesia. The subdural injection of local anaesthetic is thought to be associated with patchy anaesthesia, often unilateral and often extensive. (Haines et al., 1993).

Surrounding the dura mater is another space that is often used by anesthesiologists, the epidural space. The spinal epidural space extends from the foramen magnum to the sacral hiatus and surrounds the dura mater anteriorly, laterally, and more usefully, posteriorly. The epidural space is bounded anteriorly by the posterior longitudinal ligaments, laterally by the pedicles and intervertebral foramina, and posteriorly by the ligamentum flavum. Contents of the epidural space include the nerve roots that traverse it from foramina to peripheral locations, as well as fat, areolar tissue, lymphatics, and blood vessels, including the well-organized Batson venous plexus. Hogan suggests from his study of frozen cryomicrotome cadaver sections that the epidural space is more segmented and less uniform than previously believed from indirect anatomic analysis. This lack of epidural space uniformity also extends to age-related differences. There is evidence that adipose tissue in the epidural space diminishes with age. (Igarashi, et al., 1997).

The epidural (extradural or peridural) space in the spinal canal is that part not occupied by the dura and its contents. It extends from the foramen magnum to end by the fusion of its lining membranes at the sacrococcygeal membrane. It contains fat, nerve roots, blood vessels and lymphatics. The posterior aspect of the space is limited by the laminae
and overlying ligamentum flavum, at the sides by the pedicles of the vertebral arches and the intervertebral spaces. The front of the space is formed by the bodies of the vertebrae, the intervertebral discs and the posterior longitudinal ligament. The ligamentum flavum is 2–5 mm thick in cadavers and is divided by the vertebral spines into two parts, one arising from each lamina. The segmental structure of the epidural space has been demonstrated using contrast radiography and magnetic resonance imaging (MRI). (Dean & Mitchell, 2002).

The wedge-shape nature of each segment is especially marked in the midline. Lateral X-ray studies following the injection of radiocontrast media demonstrate a saw-tooth pattern of the epidural space. These studies suggest that the space is three to four times larger at the caudal than the cephalic part of each segment. (Ellis et al., 2004).

However, MRI studies have shown the lower end of the space in each segment to be about 4 mm wide compared to 6 mm at the upper end. This finding is in agreement with measurements made in cadavers. These differences illustrate the potential distortion due to the distensibility of this space after the injection of fluids. However, fibrous bands (sufficient to divert an epidural catheter), do stretch from the dura to the ligamentum flavum in a haphazard manner. The capacity of the epidural space is far greater than that of the subarachnoid space at the same level. Thus, in the lumbar region, 1.5–2 ml of local anaesthetic is needed to block one spinal segment by the epidural route and only 0.3 ml to produce a similar extent of block by injection into the subarachnoid space. Each spinal nerve as it passes through its intervertebral foramen into the paravertebral space carries with it a collar of the fatty areolar tissue of the epidural space. (Newell, 1999).
Pressure changes are most pronounced in the thoracic region but are elsewhere progressively dissipated by the buffering of the epidural fat, so that a negative pressure is no longer recorded within the cervical or sacral limits of the space. However, it has been argued that the negative pressure in the epidural space is produced, at least in part, by the tenting of the dura produced when a blunt epidural needle presses against the dura during insertion. (Ellis et al., 2004).

Another anatomic change in epidural space anatomy that has long been promoted is that the intervertebral foramina decrease in size with increasing age. This decrease has been linked conceptually to higher block levels for similar epidural doses of local anesthetic. Saitoh and coworkers showed that this concept is probably wrong because they could find no correlation between leakage of radiocontrast material through the intervertebral foramina and age. (Saitoh, et al., 1995).

When the data of Igarashi and associates and Saitoh and colleagues are considered together, it may be that the decrease in epidural space adipose tissue with age may dominate the age-related changes in epidural dose requirements. Unique insights into the epidural space are covered eloquently by Bernards. Posterior to the epidural space is the ligamentum flavum (the so-called yellow ligament), which also extends from the foramen magnum to the sacral hiatus. Although classically portrayed as a single ligament, it is really composed of two ligamenta flava, the right and the left, which join in the middle and form an acute angle with a ventral opening. (Hogan, et al., 1991).

The ligamentum flavum is not uniform from skull to sacrum, nor even within an intervertebral space. Ligament thickness, distance to the dura, and skin-to-dura distance vary with the area of the vertebral canal. The two ligamenta flava are variably joined (fused) in the midline, and
this fusion or lack of fusion of the ligamenta flava even occurs at
different vertebral levels in individual patients. *(Williams et al., 1989)*.

Immediately posterior to the ligamentum flavum are the lamina and
spinous processes of vertebral bodies or the interspinous ligaments.
Extending from the external occipital protuberance to the coccyx
posterior to these structures is the supraspinous ligament, which joins the
vertebral spines. Occasionally, clinically unilateral anesthesia may follow
an apparently adequate epidural technique. Hogan has also shown in
cadavers that spread of solution after epidural injection into tissues of the
epidural space is nonuniform, and he postulated that this accounts for the
clinical unpredictability of epidural drug spread.*(Hogan, 2002)*.

The epidural space can be entered by a needle passed either
between the spinal laminae or via the sacral hiatus. The spinal canal is
roughly triangular in cross-section and therefore the space is deepest in
the midline posteriorly. In the lumbar region, the distance between
the laminae to the posterior aspect of the cord is about 5 mm. The distance
from the skin to the lumbar epidural space varies between 2 cm and 7 cm,
the range in the majority of patients being 3–5 cm.*(Williams et al.,
1989)*.

The epidural space contains a network of veins. These run mainly
in a vertical direction and form four main trunks: two lie on either side of
the posterior longitudinal ligament and two posteriorly, in front of the
vertebral arches. These trunks communicate freely by venous rings at
each vertebral level. In addition, they receive the basivertebral veins,
which emerge from each vertebral body on its posterior aspect, and
communicating branches from the vertebral, ascending cervical, deep
cervical, intercostal, lumbar, ilio-lumbar and lateral sacral veins that enter
serially through the intervertebral and sacral foramina. (Ellis et al., 2004).

The epidural veins are valveless (‘the valveless, vertebral, venous plexus of Bateson’) and form a connecting link between the pelvic veins below and the cerebral veins above a possible pathway for the spread of both bacteria and malignant cells. The increase in CSF pressure that accompanies coughing and straining results in part from the shunt of blood from thoracic and abdominal veins into these thin-walled vertebral veins. The veins of the epidural space will therefore be distended if thoracic or abdominal pressure is increased, thus making a ‘bloody tap’ more likely (Williams et al., 1989). The arteries of the epidural space are relatively insignificant and originate from the arteries corresponding to the named veins enumerated above. The arteries enter at each intervertebral foramen, lie chiefly in the lateral part of the epidural space and supply the adjacent vertebrae, ligaments and spinal cord (Newell, 1999).

![Fig. (3): Tuffier's line (Inter-Cristal line)](image)

Site of lumber epidural needle insertion (L4-L5) or (L3-L4) as shown in figure (3).
Functionally, however, local anesthetics can diffuse intracranially during excessively high epidural block. Caudally, the epidural space ends at the sacral hiatus which is closed by the sacrococcygeal ligament. The epidural space contains loose areolar connective tissue, semiliquid fat, lymphatics, arteries, an extensive plexus of veins, and the spinal nerve roots as they exit the dural sac and pass through the intervertebral foramina. Investigators have defined the anatomy of the epidural space using anatomical dissection, epidural injections of resins, MRI, CT epidurography, epiduroscopy in cadavers and patients, and most recently by cryomicrotome sectioning in cadavers frozen soon after death. Now considered the gold standard of anatomic investigation due to the minimal amount of artifact associated with the technique, cryomicrotome sectioning has resulted in findings that differ from previous studies (Hogan, 1991).

Fig. (4): Midline Sagittal View Of The Lumbar Spine (Gray's anatomy 1989).

Areas of epidural fat under the ligamentum flavum extend under the laminae but are separated by areas where the posterior dura contacts,
but does not adhere to, the periosteum of the lamina. This segmentation may impede the passage of an epidural catheter and promote coiling and misplacement. Contact with the pedicles also divides the posterior epidural space from the lateral epidural space. The anteroposterior dimension of the posterior space is greatest in the lumbar region and averages 5.0 - 6.0 mm in adult males. In the thoracic region the anteroposterior dimension of the posterior epidural space decreases but the space becomes more continuous. A thin layer of epidural fat extends between the lamina and the dura. Epidural catheters placed thoracically may pass easier because areas where the dura meets bone are fewer. In more cephalad cervicothoracic regions, the epidural fat disappears and the dura directly contacts lamina. The shallow space provides little room for excessive needle advancement. A delicate smooth capsule surrounds the fat and attaches it to the dorsal midline through a connective tissue pedicle. Typically, the capsule glides freely against the surface of the lamina and ligamentum flavum, but occasionally sends attachments to the spinal roots and dura. The fat pad may absorb local anesthetics when an epidural needle and catheter are introduced directly into it using a midline approach through the pedicle (Ellis et al., 2004).

When the epidural space is entered off the midline, however, local anesthetics likely spread in the tissue planes around the fat pad and dissect the capsule away from the boney and ligamentous walls of the spinal canal. These differences may account for some of the variability in response observed with epidural anesthetics (Hogan, 1991).

The intervening pedicle in contact with the dura separates the lateral epidural space from the posterior epidural compartment. Spinal roots, septated fat, and vessels fill the space. The space typically communicates freely with the paravertebral space through the intervertebral foramina. The open intervertebral foramina transmits
intrabdominal pressure directly to the epidural space. Degenerative joint
disease and aging can narrow the intervertebral foramina and prevent the
spread of local anesthetic out the foramina, resulting in greater
longitudinal spread of local anesthetics in the epidural space (Williams et
al., 1989).

The anterior dura adheres tightly to the posterior longitudinal
ligament, which stretches across the intervertebral discs to form the
anterior epidural space between the posterior longitudinal ligament and
the periosteum of the vertebral body. The dura and posterior longitudinal
ligament blend with the annular ligament, dividing the anterior epidural
space into vertical compartments at each vertebral level. In areas
immediately next to the intervertebral discs, dense connective tissue
extensions extend superiorly and inferiorly, further dividing the anterior
epidural space into lateral halves. In lumbar but not midvertebral levels, a
membranous extension of the posterior longitudinal ligament joins with
the neural elements laterally and isolates the anterior epidural space from
the posterior and lateral epidural space (Newell, 1999).

A rich venous plexus surrounded by minimal amounts of fat almost
entirely fills the anterior epidural space. In the thoracolumbar region (T10-
L2) the basivertebral vein originates from this venous plexus and
extends into the vertebral bodies. As the size of the dural sac relative to
the epidural space decreases at the L4-L5 level, the posterior longitudinal
ligament falls away from the anterior dura, and fat fills the anterior
epidural space. The increasing amounts of epidural fat anteriorly may
contribute to the long latency of epidural anesthesia typically observed in
the L5 and S1 nerve roots. (Hogan, 1991).

The pia and arachnoid membranes continue with the spinal nerve
roots as they leave the spinal cord and exit through the intervertebral
foramina, where they blend with the perineurium of the spinal nerves.
The dura mater also extends over the nerve roots laterally, but becomes much thinner and blends with the connective tissue of the epineurium. Spinal arteries, veins, and lymphatics pierce the dura in this region as they pass to the spinal cord through the subarachnoid space (Williams et al., 1989).

The lateral halves of the ligamenta flava meet variably in the midline at an angle less than 90 degrees and form a steeply arched roof over the lumbar posterior epidural space. A midsagittal gap between the ligamenta flava in the midline is common in the thoracic and cervical regions, where it occurs in half of the segments. The midsagittal gap may contribute to a variable loss of resistance when the midline approach is used to enter the epidural space, although advancing a needle through the interspinous ligament probably produces a loss of resistance despite the absence of the ligamentum flavum.

Chromically increased intraabdominal pressure or obstruction of the inferior vena cava (as in late trimester pregnancy or in the presence of a large intraabdominal tumor) can distend the epidural venous plexus, with important implications for epidural anesthesia. This increases the risk of intravascular cannulation with an epidural catheter. It effectively decreases epidural space volume, allowing local anesthetics to distribute more widely with resulting greater degrees of block. Exposure to greater vascular surface area also potentially increases the risk for local anesthetic toxicity due to absorption from the epidural space (Ellis et al., 2004).

**Anatomy Of Lumbar Plexus And Femoral Nerve**
The lumbar plexus is derived from the anterior primary rami of the 1st, 2nd, 3rd and part of the 4th lumbar nerve roots. About 50% of subjects receive an additional contribution from T12. In much the same way as the brachial plexus, the lumbar plexus may be pre-fixed, with its lowest contribution from L3, or post-fixed, when it extends to L5 (Enneking et al, 2005).

The plexus assembles in front of the transverse processes of the lumbar vertebrae within the substance of the psoas major. L1, joined in 50% of cases by a branch from T12, divides into an upper and lower division. The upper division gives rise to the iliohypogastric and ilioinguinal nerves; the lower joins a branch from L2 to form the genitofemoral nerve. The rest of L2, together with L3 and the contribution to the plexus from L4, divide into dorsal and ventral divisions. Dorsal divisions of L2 and L3 form the lateral cutaneous nerve of the thigh and L2–L4 form the femoral nerve. The ventral branches join into the obturator nerve. (Winnie, et al.1973)
(L2–L4) and, when present, the accessory obturator nerve (L3 and L4).

Summary of branches of the lumbar plexus

- Iliohypogastric L1
- Ilio-inguinal L1
- Genitofemoral L1, 2
- Dorsal divisions
lateral cutaneous nerve of thigh L2, 3
femoral nerve L2–4
Ventral divisions
obturator nerve L2–4
accessory obturator nerve L3, 4
In addition, muscle branches are given to:
1 psoas major;
2 psoas minor;
3 iliacus;
4 quadratus lumborum

The intimate relations of the plexus to the psoas major should be noted the obturator nerve, and the accessory obturator when this is present, emerge on its medial border, the genitofemoral pierces the muscle to lie on its anterior surface, and the remaining nerves appear seriatim along the lateral border (Williams et al., 1989).
Fig. (8): Nerve supply of the thigh

1. Cutaneous femoral nerve
2. Femoral nerve
3. Obturator nerve
4. Femoral artery
5. Psoas muscle
6. Iliac muscle
7. Lumbar quadratus muscle

The femoral nerve, formed by the dorsal divisions of the anterior rami of L2–L4, is the largest terminal branch of the lumbar plexus. It travels through the psoas muscle, leaving the psoas at its lateral border. The nerve then descends caudally into the thigh via the groove formed by the psoas and iliacus muscles, entering the thigh beneath the inguinal ligament. After emerging from the ligament, the femoral nerve divides into an anterior and posterior branch. At this level it is located lateral and posterior to the femoral artery. The anterior branch provides motor innervation to the sartorius and pectineus muscles and sensory innervation to the skin of the anterior and medial thigh. The posterior branch provides motor innervation to the quadriceps muscle (rectus femoris, vastus intermedius, vastus lateralis and vastus medialis) and sensory innervation to the medial aspect of the lower leg via the saphenous nerve. The anatomic location of the femoral nerve makes this
block one of the easiest to master because the landmarks are usually simply identified (except in cases of morbid obesity), the patient remains supine, and the depth of the nerve is relatively superficial (Enneking et al, 2005).

The femoral nerve (L2–4) is the largest nerve of the lumbar plexus and, in brief, supplies the muscles and the skin of the anterior compartment of the thigh. The nerve emerges from the lateral margin of psoas, passes downwards in the groove between psoas and iliacus (to both of which it sends a nerve supply), then enters the thigh beneath the inguinal ligament. At the base of the femoral triangle, the nerve lies on iliacus, a finger’s breadth lateral to the femoral artery, from which vessel it is separated by a portion of the psoas. (Ellis et al., 2004).
Fig. (9): Somatic neurotomal distribution of the lower extremity. (Brown DL. Atlas of Regional Anesthesia.)

Fig. (10): Anatomy of femoral canal
The femoral nerve lies deep to the fascia iliaca, which in turn lies deep to the fascia lata. Note that the femoral artery and vein are situated in a separate fascia sheath.

Reprinted from Grants Atlas of Anatomy

Almost at once within the triangle the nerve breaks up into its terminal branches which stem from an anterior and posterior division

Anterior division

Muscular branches to:
1 pectineus;
2 sartorius.

Cutaneous branches:
1 intermediate cutaneous nerve of thigh;
2 medial cutaneous nerve of thigh.

Posterior division

Muscular branches to quadriceps femoris.

Cutaneous branches: asaphenous nerve.

Articular branches to:
1 hip;
2 knee.

The nerve to pectineus passes behind the femoral sheath, in which is contained the femoral artery and vein, and enters the anterior surface of the pectineus. This muscle receives in addition an inconstant supply from the accessory obturator nerve. (Ellis et al., 2004).

The nerve to sartorius arises either from, or in common with, the intermediate cutaneous nerve of the thigh, and enters the medial aspect of sartorius in its upper third. The intermediate cutaneous nerve of the thigh divides into two branches which supply the front of the thigh down to the knee. The medial cutaneous nerve of the thigh passes medially across the femoral vessels and then divides into anterior and posterior branches. The
anterior branch pierces the deep fascia at the lower third of the thigh to supply the skin over the medial side of the lower thigh as far as the knee; here the nerve links up with the patellar plexus. (Williams et al., 1989).

The posterior branch runs along the posterior border of sartorius, supplying twigs to the overlying skin and communicating with the obturator and saphenous nerves. At the knee, the nerve pierces the deep fascia and supplies an area of skin over the medial side of the leg, an area which is inversely proportional to the contribution from the obturator nerve. (Note that the lateral, intermediate and medial cutaneous nerves penetrate the deep fascia in echelon, roughly along the oblique line formed by sartorius.) (Ellis et al., 2004).

The muscular branches of the posterior division of the femoral nerve supply quadriceps femoris. The nerve to rectus femoris enters the deep aspect of the muscle near its origin; rectus femoris is the only part of the quadriceps to act on the hip as well as the knee and its nerve is the only part of the quadriceps nerve supply to give a branch to the hip joint (Winnie, et al., 1973).

Local anesthetics and additives
The choice of local anesthetic for a peripheral nerve block obviously depends to some degree on the duration of the surgical procedure, although other factors are also important. Prolonged blockade for up to 24 hours often occurs with long-acting agents such as bupivacaine or ropivacaine. Although such blockade results in good postoperative pain relief for an inpatient, it may be undesirable for an ambulatory patient because of the possible risk of nerve or tissue injury in a partially blocked limb. A short- or medium-acting agent, such as lidocaine or mepivacaine, may be more appropriate in the outpatient setting. Whatever drug is chosen, the total dosage should be calculated for each patient and be kept within acceptable safe limits. (Ilfeld et al., 2002).

The highest concentrations of local anesthetic drugs are not appropriate for peripheral neural blockade; therefore, 0.75% bupivacaine or ropivacaine, 2% lidocaine, 2% mepivacaine, and 3% 2-chloroprocaine are not recommended. Conversely, the lowest concentrations of the same agents (i.e., 0.25% bupivacaine or ropivacaine and 0.5% mepivacaine or lidocaine) may not provide complete motor blockade. (Motamed, et al., 2009).

Local anesthetics block the generation and the conduction of nerve impulses, presumably by increasing the threshold for electrical excitation in the nerve, by slowing the propagation of the nerve impulse and by reducing the rate of rise of the action potential. In general, the progression of anesthesia is related to the diameter, myelination, and conduction velocity of affected nerve fibers. Clinically, the order of loss of nerve function is as follows: pain, temperature, touch, proprioception, and skeletal muscle tone.
Systemic absorption of local anesthetics produces effects on the cardiovascular and central nervous systems. At blood concentrations achieved with normal therapeutic doses, changes in cardiac conduction, excitability, refractoriness, contractility, and peripheral vascular resistance are minimal. However, toxic blood concentrations depress cardiac conduction and excitability, which may lead to atrio-ventricular block and ultimately to cardiac arrest. In addition, myocardial contractility is depressed and peripheral vasodilation occurs, leading to decreased cardiac output and arterial blood pressure (Tucker et al., 2005).

Following systemic absorption, local anesthetics can produce central nervous system stimulation, depression, or both. Apparent central stimulation is manifested as restlessness, tremors, and shivering, progressing to convulsions, followed by depression and coma progressing ultimately to respiratory arrest. However, the local anesthetics have a primary depressant effect on the medulla and on higher centers. The depressed stage may occur without a prior excited stage (Tetzlaff et al., 2000).

**Chemistry Of Local Anesthetics**

The Local Anesthetic Molecule (The structure of local anesthetics):
The diagrams above show the essential structures of the two major types of local anesthetic agent:

- The diagram to right represents the structure of procaine (Novocain). The chain that connects the benzene ring on the left with the amide tail on the right is an "ester linkage".
- The diagram to the left represents lidocaine and its analogs. The connecting chain in this case is called an "amide linkage". The amide linkage contains an extra nitrogen to the left of the C=O (carboxyl) group.

All local anesthetics are weak bases. They all contain:

- An *aromatic group* (a lipophilic group-usually a benzene ring seen on the left side of both structures above)
- An *intermediate chain*, either an *ester* or an *amide*.
  \[
  \begin{align*}
  &\text{O (amide linkage)} & &\text{O (ester linkage)} \\
  &\text{|} & &\text{|} \\
  &\text{(-NH C-)} & &\text{(-C-O)}
  \end{align*}
  \]
- An *amine group* (hydrophilic group-usually a tertiary amine seen on the right side of both molecular structures above) (*Evers and Maze 2004*).

**Structure-Activity Relationships:**
Local anesthetics are weak bases that usually carry a positive charge at the tertiary amine group at physiologic pH. The nature of the intermediate chain is the basis of the classification of local aesthetics as esters or amides.

Physicochemical properties of local anesthetics depend upon:

1. The substitutions in the aromatic ring.
2. The type of linkage in the intermediate chain.
3. The alkyl groups attached to the amine nitrogen.

I-Potency:

Correlates with lipid solubility; that is potency depends upon the ability of the local anesthetic to penetrate a hydrophobic environment. In general; potency and hydrophobicity increase with an increase in the total number of carbon atoms in the molecule.

More specifically, potency is increased by:

- Adding a halide to the aromatic ring (2-chloroprocaine as opposed to procaine).
- An ester linkage (procaine versus procainamide).
- Large alkyl groups on the tertiary amide nitrogen (etidocaine versus lidocaine).

Cm: is the minimum concentration of local anesthetic that will block nerve impulse conduction and is analogous to the minimum alveolar concentration (MAC) of inhalational anesthetics.

This measure of relative potency is affected by several factors including:

1. Fiber size, type and myelination.
2. pH (acidic pH antagonizes block).
3. Frequency of nerve stimulation (access of local anesthetic to the sodium receptor is enhanced by repeatedly opening the sodium channel).
4. Electrolyte concentrations (hypokalemia and hypercalcemia antagonize blockade) (*Tetzlaff, 2000*).

### Table (1) Nerve fiber classification (*Morgan et al., 2006*)

<table>
<thead>
<tr>
<th>Fiber type</th>
<th>Sensory classification</th>
<th>Modality Served</th>
<th>Diameter (um)</th>
<th>Conduction (m/s)</th>
<th>Local Anesthetic sensitivity</th>
<th>Myelination</th>
</tr>
</thead>
<tbody>
<tr>
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<td></td>
</tr>
<tr>
<td>Aα</td>
<td>Type Ia</td>
<td>Proprioception</td>
<td>12-20</td>
<td>70-120</td>
<td>++</td>
<td>Yes</td>
</tr>
<tr>
<td>Aα</td>
<td>Type Ib</td>
<td>Proprioception</td>
<td>12-30</td>
<td>70-120</td>
<td>++</td>
<td>Yes</td>
</tr>
<tr>
<td>Aβ</td>
<td>Type II</td>
<td>Touch pressure proprioception</td>
<td>5-12</td>
<td>30-70</td>
<td>++</td>
<td>Yes</td>
</tr>
<tr>
<td>Aγ</td>
<td>Motor (muscle spindle)</td>
<td>3-6</td>
<td>15-30</td>
<td>++</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Aδ</td>
<td>Type III</td>
<td>Pain Cold temperature Touch</td>
<td>2-5</td>
<td>12-30</td>
<td>+++</td>
<td>Yes</td>
</tr>
<tr>
<td>B</td>
<td>Preganglionic autonomic fibers</td>
<td>&lt;3</td>
<td>3-14</td>
<td>++++</td>
<td>Some</td>
<td></td>
</tr>
<tr>
<td>C Dorsal root</td>
<td>Type IV</td>
<td>Pain Warm and cold temperature Touch</td>
<td>0.4-1.2</td>
<td>0.5-2</td>
<td>++++</td>
<td>No</td>
</tr>
<tr>
<td>C Sympathetic</td>
<td>Postganglionic sympathetic fibers</td>
<td>0.3-1.3</td>
<td>0.7-2.3</td>
<td>++++</td>
<td>No</td>
<td></td>
</tr>
</tbody>
</table>

**II-Onset of action:**

Depends upon many factors including the relative concentration of the nonionized lipid-soluble form (B) and the ionized water-soluble form (BH⁺). The pH at which the amount of ionized and nonionized drug is equal is the pKa of the drug. For instance, the pKa of lidocaine is 7.8.
When lidocaine is exposed to a higher hydrogen ion concentration (e.g. a pH of 7.4) more than half of it will exist as the charged cation form (BH\(^+\)). Although both forms of local anesthetic are involved in blockade, only the lipid-soluble form diffuses across the neural sheath (epineurium) and nerve membrane. Local anesthetics with a pKa closer to physiologic pH will have a higher concentration of nonionized base that can pass through the nerve cell membrane and onset will be more rapid. Once inside the cell the nonionized base will reach equilibrium with its ionized form. Only the charged cation actually binds to the receptor within the sodium channel. Not all local anesthetics exist in a charged form (e.g. benzocaine), however. These anesthetics probably act by an alternative mechanism (e.g. expanding the lipid membrane). Onset of action of local anesthetics in isolated nerve fiber preparations directly correlates with pKa. However, clinical onset of action is not necessarily identical for local anesthetics with the same pKa. Other factors, such as ease of diffusion through connective tissue, can affect the onset of action in vivo (*Courtney and Strichartz, 1987*).

**III-Duration of action:**

It is associated with plasma protein binding (α\(_1\)-acid glycoprotein), presumably because the local anesthetic receptor is also a protein. The pharmacokinetic factors that determine absorption also affect duration of action.

**Mechanisms Of Action Of Local Anesthetics**

**Theories Of Local Anesthetic Action:**

Local anesthetics cause a reversible block to the conduction of impulses along nerve fibers. Although local anesthetics alter potassium and calcium ion conductance across excitable membranes, inhibition of
sodium ion influx across the neuronal cell membrane is the common mechanism of action through which all local anesthetic agents produce blockade of the nerve impulse (Courtney and Kendig, 1988).

Since a wide variety of chemical compounds exhibit local anesthetic activity, it is unlikely that they all block sodium conductance in the same manner. Several theories regarding the mechanism of action of local anesthetics include:

I-The Specific Receptor Hypothesis:

The most popular theory regarding the mechanism of action of local anesthetics proposes that they interact directly with specific receptors in the neuronal membrane (Strichartz, 1973). These receptors, in turn, affect specific ion channels of the neuronal membrane in such a fashion that the ionic flux needed for initiation and propagation of the action potential is inhibited.

The Voltage-gated Na\textsuperscript{+} Channel

Ion channels (Catterall, 2000) are a class of proteins that span the cell membrane and a) conduct ions, b) do so selectively, and c) respond to electrical, mechanical and chemical signals by opening or closing. The selectivity of channels allows permeability through the sodium channel to be 20-fold greater for sodium than for potassium. The probability of the channel being open or closed is controlled by gating:

- Chemical gating produces a change in the channel in response to a transmitter, such as the opening of the ACh sensitive Na\textsuperscript{+} channel at the motor endplate.
- Mechanical gating takes place at nerve ends in response to touch or pressure.
- A voltage gated channel opens and closes in response to changes in
the membrane potential. The duration the channel remains open is fixed for that channel.

Figure (12) Structure of the neuronal cell membrane (Malamed, 1997)

The architecture for all types of channels consists of four to six subunits formed around a water-filled pore. The more the subunits, the larger the pore and the less selective the channel for the ions which pass. The voltage-gated channels are made of 4 units and are highly selective. The channel is formed from a single protein that has four repeated domains corresponding to four channel subunits, each with six transmembrane segments.
Figure (13:) Structure of a Na\(^+\) channel -subunit. (A) Schematic diagram of the four domains DI–DIV. Each domain consists of six segments, which span the membrane. Part of the ‘pore’ loops, the amino acid links between the S5 and the S6 segments are symbolized as red triangles. These four amino acid links ‘DEKA’ form the selectivity filter in the outer pore mouth (for more details see section Structure of Na\(^+\) channel). (B) 3D sketches of a Na\(^+\) channel with top and bottom views and large cross-section as derived from data of cryo-electron microscopy and single particle analysis. On the left side of the large cross-section the cut is through the S4 segment (the function of the cavity marked in red is unclear) and on the right side the cross-section is through the S6 segment overlaid with the amino acid sequence of rat brain Na\(^+\) channel (Na\(_v\) 1.2). Residues that are coloured and numbered (60 for amino acid 1760 etc.) are important for the affinity of local anaesthetics. (Adapted from Catterall, 2001 and Scholz, 2002)
Figure (14) Representation of the local anesthetic binding to the sodium channel (Haas, 2002)

The voltage-gated Na\(^+\) channel produces the action potential by opening in response to membrane depolarization, producing an influx of Na\(^+\), which in turn produces more depolarization. The change in electrical field around the channel causes a conformational change, opening or closing the pore. Each subunit has a helical section with a basic amino acid in every third position along the helix, which probably represents a voltage-sensing device. Depolarization causes a tilting of the subunits and a torsional movement of the channel units akin to the opening of the iris in a camera, accompanied by a tiny outward shift of charge (the gating current). The channels then close by time- and voltage-dependent mechanisms. After closing, the channel is unresponsive to depolarization; the inactivation of many channels after depolarization makes the membrane refractory. Thus, the voltage-gated Na\(^+\) channel exists in three states: Resting, in which it is closed to ion flux but will respond to depolarization by opening. Open, allowing ion flux. Inactive, which is closed and can only open after returning to the resting state.
Voltage-gated Na\(^+\) channels in nerve membrane open quickly and briefly after a depolarizing stimulus, whereas those in muscle, including heart, may have sustained bursts of openings which may contribute to the prolonged action potential of the heart. Following this sustained opening, a more prolonged inactivation ensues.

The distribution of the population of sodium channels between the resting and inactivated states is an important determinant of the refractory behavior of neurons. Immediately following an action potential, many of the sodium channels are in the inactivated state and cannot be reopened by a subsequent voltage change. Therefore, once an excitable membrane has been depolarized by an action potential, it cannot conduct a second impulse until it has first repolarized and thereby allowed inactivated sodium channels to return to the resting state. If an adequate number of sodium channels are not present in the resting state, sodium current sufficient for a second action potential cannot be generated (Catterall, 2001).

The property of use-or frequency-dependent blockade, in which neuronal blockade by charged local anesthetic molecules increases with
repetitive, brief membrane depolarization, is one phenomenon that suggests direct interaction between sodium channel receptors and the charged local anesthetic molecule (Courtney, 1975).

It is postulated that frequency dependence develops because charged, hydrophilic anesthetic molecules inhibit sodium ion conductance through the sodium channel by gaining access to a channel receptor, located within the channel itself, while the sodium channel pore is in the open state. Reversal of the local anesthetic inhibitory effect would also require an open channel pore to facilitate the dissociation of the local anesthetic molecule, and, thus, a closed channel containing a local anesthetic molecule would be slow to return to its uninhibited state. In contrast to charged anesthetics, neutral anesthetic compounds exhibit much less frequency-dependent blockade, and this may be the result of these molecules not being restricted to the aqueous phase, gaining access to a channel binding site through the lipid milieu of the membrane interior.

Local anesthetics may also shift the sodium channel population to a nonconducting state by binding preferentially to channels that have already been inactivated, preventing their return to the resting, depolarization-susceptible configuration (Hollmann et al., 2001).

In addition to interacting with sodium channels that are in the open and in the inactivated state it appears that local anesthetics can also produce a tonic, or resting, block by binding with the channels in the resting state to prevent their voltage-induced activation (Strichartz and Bered, 2005).

The variable state of the local anesthetic receptor determines the strength of its interaction with the local anesthetic molecule, and an excitable membrane with a higher depolarization frequency is more sensitive to the blocking effects of local anesthetics. The charged local
anesthetics interact with all three sodium channel states, and the resultant variable drug potency is manifested as frequency-dependent blockade. Use or frequency dependence may be a mechanism by which a local anesthetic solution causes a differential blockade of the fibers within a given nerve. It is uncertain as to where exactly the local anesthetic receptors of the sodium channel are located, and there may be at least three sites of local anesthetic binding:

- One is located near the interior opening of the sodium pore and has a higher affinity for the more charged local anesthetic molecules.
- One is located at the interface between the sodium channel structure and the surrounding membrane lipid, being more easily accessed by uncharged, lipophilic local anesthetic molecules (Strichartz & Bered, 2005).
- In addition, there are a variety of other sodium channel sites where certain pharmacologic compounds and toxins specifically combine. Tetrodotoxin, produced by several species of puffer fish and frogs, and saxitoxin, produced by a marine dinoflagellate, are examples of other molecules that specifically bind to sodium channels. They directly interact with the outer aspect of the sodium channel to block sodium conductance (Akopian et al., 1999).
Local anesthetics may also block calcium and potassium channels and N-methyl-D-aspartate (NMDA) receptors to varying degrees. Differences in these additional actions may be responsible for clinically observed differences between agents. Conversely, other classes of drugs, most notably tricyclic antidepressants (amitriptyline), meperidine, volatile anesthetics, and ketamine also have sodium channel-blocking properties (Sugimoto et al., 2003).

II-The Calcium Displacement Hypothesis:

Displacement of calcium from a membrane site that controls sodium permeability has been proposed as a mechanism of local anesthetic activity (Blausteine and Goldman, 1966). A low calcium ion concentration outside the neuron enhances local anesthetic activity, and an increasing external calcium concentration antagonizes the blocking action of local anesthetic. However, the direct actions of calcium and local anesthetics appear to be independent of each other (Strichartz, 1976). Thus, it is unlikely that calcium directly mediates the activity of local anesthetic agents.

III-The Membrane Perturbation Hypothesis:

This involves an application of the Meyer-Overton rule of anesthesia. It postulates that diffusion of the relatively lipophilic anesthetic molecules into the lipid component of the neuronal membrane
expands the membrane to a critical volume and interferes with sodium conductance. Decreased sodium permeability could occur either through an increase in the lateral pressure in the membrane, which would directly compress the sodium channels, or through a conformational change in the proteins of the sodium channels brought about by an increase in the degree of the disorder of the membrane lipid molecules. Local anesthetic agents have been shown both to increase the volume of lipid membranes and to increase their degree of disorder and thus, fluidity (Seeman, 1975).

High-pressure antagonism of the anesthetic activity of certain uncharged local anesthetic molecules, such as benzyl alcohol and benzocaine, has been shown to occur by some investigators and may be evidence for the applicability of the membrane expansion theory to the mechanism of action of these compounds (Kendig and Cohen, 1977). However, pressure reversal has not been shown to occur in the case of charged local anesthetics, and there is no direct evidence that membrane expansion is important in their activity. These findings, as well as others, indicate that charged and uncharged local anesthetic molecules may have separate sites of action and that membrane expansion may be more important for the action of only the uncharged local anesthetics (Mrose and Ritchie, 1978).

IV-The Surface Charge Theory:

Because some of the neuronal membrane molecules contain hydrophilic, anionic tails that are arrayed so that they protrude outward from the membrane lipid to both the external (extracellular) and internal (axoplasmic) surfaces of the membrane, both surfaces of the axolemma are negatively charged relative to the membrane interior (Hille, 1968).
These fixed negative charges attract cations such as sodium and calcium, and these charge interactions add to the electrochemical resting potential to yield the net transmembrane potential. The fixed negative charges of the membrane’s two surfaces may also attract cationic local anesthetic molecules, aligning the charged local anesthetic molecule at the membrane-water interface with its nonpolar aromatic domain in the membrane lipid and its hydrophilic, charged portion in the adjacent aqueous phase. The cationic local anesthetic molecule thus neutralizes the fixed negative charges on the membrane surface to a variable degree and alters the transmembrane potential (*Mclaughlin, 1975*).

If the local anesthetic molecule is absorbed to the extracellular side of the axonal membrane, the extra positive charges there could add to the already relatively positive extracellular charge and hyperpolarize the membrane, resulting in it being more difficult for an approaching nerve impulse to raise the transmembrane potential to depolarization threshold. On the other hand, if the local anesthetic molecule is absorbed into the intracellular side of the axonal membrane, the increase in positive charge could prevent sufficient repolarization of the membrane interior to allow for reactivation of sodium channels inactivated by a previous action potential. If sufficient sodium channels remain in the inactivated state, a subsequent action potential could not occur. Either mechanism could produce neural blockade (*Wei, 1969*).

The surface charge theory has the support of several investigators and also accounts for the antagonism between divalent actions, such as calcium, and local anesthetic compounds. Although the surface charge hypothesis may account for the action of charged local anesthetics, it does not explain the ability of uncharged local anesthetics, such as benzyl alcohol and benzocaine, to block nerve impulses. However, the failure of
a single theory to satisfactorily explain the actions of all local anesthetics does not necessarily invalidate it. Different local anesthetic molecules may have different mechanisms of action (Blaustein and Goldman, 1966).

Pharmacokinetics Of Local Anesthetics

The concentration of local anesthetics in blood is determined by the amount injected, the rate of absorption from the site of injection, the rate of tissue distribution, and the rate of biotransformation and excretion of the specific drug. Patient-related factors such as age, cardiovascular status, and hepatic function influence the physiologic disposition and the resultant blood concentrations of local anesthetics (Strichartz and Berde, 2005).

Absorption:

The systemic absorption of local anesthetics is determined by:

1. Site of injection:

A comparison of the blood concentration of local anesthetics following various routes of administration reveals that the anesthetic drug level is highest after intercostal nerve blockade, followed in order of decreasing concentration by injection into the caudal epidural space, lumbar epidural space, brachial plexus site, subarachnoid space and subcutaneous tissue (Tucker and Mather, 2005).

When a local anesthetic solution is exposed to a greater vascular area, this results in a greater rate and degree of absorption. This relationship of administration site to rate of absorption is of clinical significance, since use of fixed dose of a local anesthetic agent may be potentially toxic in one area of administration but not in others. For example, the use of 400 mg of lidocaine without epinephrine for intercostal nerve block results in an average peak venous plasma level of
approximately 7 μg/ml, which is sufficiently high to cause symptoms of central nervous system toxicity in some patients. This same dose of lidocaine employed for brachial plexus block yields a mean maximum blood level of approximately 3 μg/ml, which is rarely associated with signs of toxicity (Covino and Wildsmith 1998).

2. Dosage:

For most local anesthetic agents, a linear relationship exists between the amount of drug administered and the resultant peak venous plasma level. The mean venous plasma level of lidocaine increases from approximately 1.5 to 4 μg/ml as the total dose administered into the lumbar epidural space is increased from 200 to 600 mg. Depending on the site of administration, a peak blood level of 0.5 to 2 μg/ml is achieved for each 100 mg of lidocaine or mepivacaine injected (Covino and Wildsmith 1998).

3. Addition of a vasoconstrictor agent:

In general, the addition of epinephrine to local anesthetic solutions decreases the rate of vascular absorption of these agents. 5μg/ml of epinephrine (1:200,000) significantly reduces the peak blood levels of lidocaine and mepivacaine, regardless of the site of administration. However, peak blood levels of bupivacaine and etidocaine are minimally influenced by the addition of epinephrine following injection into the lumbar epidural space. On the other hand, the rate of vascular absorption of these agents is significantly decreased when epinephrine-containing solutions are employed for brachial plexus blockade (John and Butterworth, 2006).

4. Pharmacologic profile of the agent:

The rate of vascular absorption also varies depending on the specific local anesthetic agent. For example, lidocaine is absorbed more
rapidly following brachial plexus and epidural blockade than is prilocaine, whereas bupivacaine is absorbed more rapidly than etidocaine.

Prilocaine is a less potent vasodilator than lidocaine, which partly accounts for the lower blood levels of prilocaine. The lower peak blood levels of etidocaine compared with bupivacaine may be related to the greater lipid solubility of etidocaine, which results in its sequestration by adipose tissue and a decreased rate of absorption. The differences in absorption rates are of practical clinical significance, since they permit the use of larger doses of prilocaine compared with lidocaine and etidocaine compared with bupivacaine (Tetzlaff, 2000).

**Distribution:**

Distribution depends upon organ uptake, which is determined by the following factors:

1. **Tissue perfusion:**

   The distribution of local anesthetic agents can be described by a tow- or three-compartment model.

   - The rapid disappearance (α phase) is believed to be related to uptake by rapidly equilibrating tissues, that is, tissues with a high vascular perfusion (brain, lung, liver kidney, and heart).
   - The slower phase of disappearance from blood (β phase) is mainly a function of distribution to slowly equilibrating tissues (muscle and gut) and the biotransformation and excretion of the compound.

   The α half-life (t1/2 α) of prilocaine is shorter than that of lidocaine and mepivacaine, which indicates that prilocaine is redistributed at a significantly more rapid rate from blood to tissues than the other two drugs (Tucker and Mather, 2005). The t1/2 α of lidocaine and mepivacaine are similar. In addition, the half-life of the β disappearance
phase ($t_{1/2} \beta$) of prilocaine is more rapid than that of lidocaine and mepivacaine, suggesting a more rapid rate of biotransformation. A comparison of bupivacaine and etidocaine reveals that etidocaine has a more rapid rate of tissue redistribution and biotransformation than does bupivacaine.

**Table (2) Distribution of local anesthetics (Tucker and Mather, 2005)**

<table>
<thead>
<tr>
<th>Agent</th>
<th>$t_{1/2}\alpha$ (min)</th>
<th>$t_{1/2}\beta$ (min)</th>
<th>$V_{Ds}$ (L)</th>
<th>$t_{1/2}\gamma$ (h)</th>
<th>CI (L/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prilocaine</td>
<td>0.5</td>
<td>0.5</td>
<td>261</td>
<td>1.5</td>
<td>2.84</td>
</tr>
<tr>
<td>Lidocaine</td>
<td>1.0</td>
<td>9.6</td>
<td>91</td>
<td>1.6</td>
<td>0.95</td>
</tr>
<tr>
<td>Mepivacaine</td>
<td>0.7</td>
<td>7.2</td>
<td>84</td>
<td>1.9</td>
<td>0.78</td>
</tr>
<tr>
<td>Bupivacaine</td>
<td>2.7</td>
<td>28.0</td>
<td>72</td>
<td>3.5</td>
<td>0.47</td>
</tr>
<tr>
<td>Etidocaine</td>
<td>2.2</td>
<td>19.0</td>
<td>133</td>
<td>2.6</td>
<td>1.22</td>
</tr>
<tr>
<td>Ropivacaine</td>
<td>2.1</td>
<td>14.0</td>
<td>41</td>
<td>1.8</td>
<td>0.44</td>
</tr>
</tbody>
</table>

As $t_{1/2} \alpha = \alpha$ half-life ...... $t_{1/2} \beta = \beta$ half-life.... $t_{1/2} \gamma = \gamma$ half-life

CI=Clearance Index $V_{Ds}$= Volume of Distribution

Local anesthetic agents are distributed throughout all body tissues, but the relative concentration in different tissues varies as a function of time, vascular perfusion, and tissue mass. Initially, local anesthetic agents are rapidly extracted by lung tissue so that the whole blood concentration of local anesthetics decreases greatly as they pass through the pulmonary vasculature.

**2-Tissue/ blood partition coefficient:**

Strong plasma protein binding tends to retain anesthetic in the blood, while high lipid solubility facilitates tissue uptake.

**3-Tissue mass:**

Ultimately, the highest percentage of an injected dose of a local anesthetic agent is found in skeletal muscle, simply because the mass of skeletal muscle makes it the largest reservoir for local anesthetic agents (*Taheri et al., 2003*).

**Biotransformation and Excretion:**
The degradation of local anesthetic agents varies according to their chemical classification.

1- **Esters:** The esters of procaine-like drugs are hydrolyzed in plasma by *pseudocholinesterase* (*plasma cholinesterase or butyrylcholinesterase*) enzyme. Chloroprocaine shows the most rapid rate of hydrolysis (4.7 μ mole/ml/hour), compared with a rate of 1.1 μ mole/ml/hour for procaine and 0.3 μ mole/ml/hour for tetracaine. Less than 2% of unchanged procaine is found in urine, whereas approximately 90% of p-aminobenzoic acid (PABA), which is a primary product of procaine hydrolysis, appears in urine. Only 33% of diethylaminoethanol, the other hydrolysis product of procaine, is excreted unchanged.

2- **Amides:** The aminoamidine agents are metabolized primarily in the liver. Prilocaine undergoes the most rapid rate of hepatic metabolism, whereas lidocaine is metabolized somewhat more rapidly than mepivacaine. In humans the hepatic clearance of etidocaine is greater than that of bupivacaine, which suggests a more rapid rate of hepatic metabolism for etidocaine. Evidence also exists that prilocaine may be metabolized in the kidney, which would explain that rapid clearance of this agent compared with all other amino amides (*Thomas and Schug, 1999*).

The biotransformation of the amide-type agents results in the formation of a variety of metabolites. The metabolism of lidocaine has been studied most extensively. The main metabolic pathway of lidocaine in humans appears to involve oxidative deethylation of lidocaine to monoethylglycinexylidide, followed by a subsequent hydrolysis of monoethylglycinexylidide to xylidine. In humans the hepatic clearance of etidocaine is greater than that of bupivacaine, which indicates that etidocaine is metabolized in the liver more rapidly than bupivacaine (*Tetzlaff, 2000*).
The excretion of the amide-type local anesthetic drugs occurs by way of the kidney. Less than 5% of the unchanged drug is excreted via the kidney into the urine. The major portion of the injected agent appears in the urine in the form of various metabolites. The renal clearance of the amide local anesthetic agents appears to be inversely related to their protein-binding capacity. Prilocaine, which has a lower protein-binding capacity than lidocaine, has a substantially higher clearance value than lidocaine. Renal clearance also is inversely proportional to the pH of urine, suggesting that urinary excretion of these agents occurs by nonionic diffusion (Covino and Wildsmith, 1998).

Bupivacaine

Bupivacaine is a local anesthetic which blocks the generation and conduction of nerve impulses. It is commonly used for analgesia by infiltration of surgical incisions. Preemptive use of analgesics (including local anesthetics used to control post-operative pain) i.e. before tissue injury, is recommended to block central sensitization, thus preventing pain or making pain easier to control (Tucker et al., 2005).

Bupivacaine has a longer duration of action than lidocaine, to which it is chemically related - approx. 6-8 hours as opposed to 1-2 hours for lidocaine. Duration of action is affected by the concentration of bupivacaine used and the volume injected. Concentration affects the time for local anesthesia to occur and the density of the block. Volume determines the area that is infiltrated and therefore anesthetized (Tetzlaff et al., 2000).

Total dose in mg/kg is important in local anesthetic toxicity. Signs of toxicity include central nervous system signs (seizures), and cardiac dysrhythmias progressing to asystole (irreversible cardiac arrest).
Bupivacaine toxicity is dose dependent; there is variation between species and age of animals. Rats appear to be more tolerant than larger species (e.g. dogs, sheep, humans), while rabbits are thought to be more sensitive (Boogaerts et al., 1993).

Bupivacaine is a prescription drug, but it is not a controlled substance. It is available in concentrations of 0.25%, 0.5% and 0.75%, either plain or combined with epinephrine (1:200,000). Epinephrine reduces cutaneous blood flow and therefore prolongs the local anesthetic effects. Maximum concentration of bupivacaine recommended for subcutaneous use is 0.25%. Higher concentrations are used mostly for caudal and epidural blocks in human medicine. (Tucker et al., 2005).

Bupivacaine injectable (0.25%), with or without epinephrine, in single dose vials of 10mls and 30mls, or multi-dose vials of 50mls, is available from most veterinary supply houses (Tetzlaff et al., 2000).

Clonidine:

The choice of local anesthetic for continuous epidural infusion varies. In general, bupivacaine, ropivacaine, or levobupivacaine is chosen because of the differential and preferential clinical sensory blockade with minimal impairment of motor function. Concentrations used for postoperative epidural analgesia (≤0.125% bupivacaine or levobupivacaine or ≤0.2% ropivacaine) are lower than those used for intraoperative anesthesia (Curatolo, et al. 2000).

A variety of adjuvants may be added to epidural infusions to enhance analgesia while minimizing side effects, but none has gained widespread
acceptance. Two of the more studied adjuvants are clonidine and epinephrine. Clonidine mediates its analgesic effects primarily through the spinal dorsal horn $\alpha_2$-receptors on primary afferents and interneurons, as well as the descending noradrenergic pathway, and the epidural dose typically used ranges from 5 to 20 $\mu$g/hr. Clinical application of clonidine is limited by its side effects: hypotension, bradycardia, and sedation. Hypotension and bradycardia are both dose dependent. Epinephrine may improve epidural analgesia, can increase sensory blockade, and is generally administered at a concentration of 2 to 5 $\mu$g/mL. (Sakaguchi et al., 2000)

Clonidine is a selective $\alpha_2$ adrenergic agonist with some $\alpha_1$ agonist properties. Such drugs induce antinociception by activating the descending noradrenergic inhibitory system and by inhibiting synaptic transmission within the dorsal horn of the spinal cord via activation of spinal cholinergic neurons (Millar et al., 1993). Activating the $\alpha_2$ adrenoceptor triggers an inwardly rectifying potassium conductance in dorsal horn neurons, causing hyperpolarization, reduced excitability and analgesia. Spinal clonidine produces analgesia by mimicking the effect of norepinephrine on wide dynamic range neurons. This inhibition is also observed in the intermediolateral cell column, the origin of sympathetic vasoactive neurons, and causes a decrease in sympathetic outflow.

Clonidine acts synergistically with local anesthetics because of its action of opening potassium channels. The duration of both sensory and motor blockade from spinally and epidurally applied local anesthetics is prolonged (Carabine et al., 1992). Co-administration of clonidine and local anesthetics intrathecally prolongs analgesic and motor block duration, and the quality of the block is enhanced compared to intrathecal local anesthetic alone (De Kock et al., 2001). This is a dose dependent
phenomenon with a maximum effect after 75-100 µg. The type of local anesthetic does not seem to be important. The antinociceptive interaction of intrathecal clonidine and lidocaine was demonstrated in a rat model (Hao et al., 2001); isobolographic analysis showed a synergistic effect. Arterial hypotension is the most commonly reported side effect of neuroaxial use of clonidine; it is mostly due to direct inhibition of sympathetic outflow of preganglionic neurons in the spinal cord. Other side effects include sedation and a reduction of the heart rate.

Clonidine prolongs the action of local anesthetic peripheral blocks into the post-operative period. Its effect is dose-related and the minimum effective doses, which significantly prolong analgesia and anesthesia, are respectively 0.1 and 0.5 mcg/kg after brachial plexus block with mepivacaine (Singelyn et al., 1996). Clonidine opens the potassium channels, resulting in membrane hyperpolarization, a state that is unresponsive to excitatory input (Butterworth and Strichartz, 1993).

Clonidine is a frequently used adjuvant to local anesthetics (LA). The analgesic properties of clonidine when administered intrathecally or epidurally have been demonstrated; they seem to be attributable to its α₂ agonist properties. The benefit of adding clonidine to LAs for peripheral nerve blocks is less clear, although it is widely believed that clonidine improves quality and duration of a LA block. (Elia et al., 2008).
Femoral Nerve Block

During the last decade, there has been renewed interest in continuous peripheral nerve blocks (CPNBs) also called “perineural local anesthetic infusions.” These techniques involve the placement of a catheter directly adjacent to the peripheral nerve(s) supplying the surgical site and infusing a local anesthetic via the perineural catheter providing potent, site-specific analgesia. This method was first described in 1946 using a cork to stabilize a needle placed adjacent to the brachial plexus divisions to provide a “continuous” supraclavicular block. (Ansbro, 1946).

Because there are inherent risks with CPNBs, the majority of the series/studies limit these techniques to patients expected to have at least moderate postoperative pain of a duration more than 24 hours that is not easily managed with oral opioids. However, a CPNB may be used after mildly painful procedures defined here as usually well managed with oral analgesics to decrease opioid requirements and opioid-related side effects. Because not all patients desire, or are capable of accepting, the extra responsibility that comes with the catheter and pump system, appropriate patient selection is crucial for safe CPNB, particularly in the ambulatory environment. Although recommendations for the use of various catheter locations for specific surgical procedures exist, (Boezaart, 2006).

Published data specifically illuminating this issue are sparse. In general, axillary, cervical paravertebral, infraclavicular, or supraclavicular infusions are used for surgical procedures involving the hand, wrist, forearm, and elbow; interscalene, cervical paravertebral, or inter sternocleidomastoid catheters are used for surgical procedures involving the shoulder or proximal humerus; thoracic paravertebral
catheters are used for breast or thorax procedures; psoas compartment catheters are used for hip surgery; fascia iliaca, femoral, or psoas compartment catheters are used for knee or thigh procedures; and popliteal or subgluteal catheters are used for surgical procedures of the leg, ankle, and foot. The femoral nerve block provides analgesia to the anterior thigh, including the flexor muscles of the hip and extensor muscles of the knee. Historically this block was also known as the “3-in-1 block,” suggesting that the femoral, lateral femoral cutaneous, and obturator nerves could be blocked from a single paravascular injection at the femoral crease. Studies have demonstrated that the femoral and lateral femoral cutaneous nerves can be reliably blocked by a single injection, but the obturator nerve is often missed. Therefore, a posterior lumbar plexus block should be used when all three nerves need to be anesthetized (although this point remains controversial). The femoral nerve block is an ideal block for surgeries of the hip, knee, or anterior thigh and is often combined with a sciatic nerve block for near complete lower extremity analgesia. Complete analgesia of the leg can be achieved without lumbar plexus block by combining a femoral nerve block with parasacral sciatic nerve block (which blocks the obturator over 90% of the time), or by adding an individual obturator nerve block to the femoral nerve block. Only limited published data are available regarding the balancing of potential risks and benefits of perineural infusion for patients with significant comorbidities. Investigators often exclude patients with known hepatic or renal insufficiency in an effort to avoid local anesthetic toxicity. For CPNBs that may inhibit the phrenic nerve and ipsilateral diaphragm function (e.g., interscalene or cervical paravertebral catheters), patients with heart or lung disease are often excluded because interscalene blocks and infusions have been shown to cause frequent ipsilateral diaphragm paralysis. Although the effect on overall pulmonary
function may be minimal for relatively healthy patients, practitioners must be aware of the possible related risks and be prepared to manage complications. The femoral nerve is formed within the psoas major muscle by posterior divisions of the second, third, and fourth lumbar nerves. It emerges from the lateral border of the psoas muscle, descends in the groove between the psoas and iliacus muscles, and enters the thigh by passing beneath the inguinal ligament lateral to the femoral artery. At this point the nerve divides into multiple terminal branches, which have been classified as anterior and posterior (Allen et al., 1998).

The anterior branches are primarily cutaneous, and the deep branches are chiefly motor. The femoral nerve supplies the anterior compartment muscles of the thigh (i.e., quadriceps, sartorius) and the skin of the anterior aspect of the thigh from the inguinal ligament to the knee. Its terminal branch is the *saphenous nerve*, which supplies an area of skin along the medial side of the leg from the knee to the bigtoe (Allen et al., 1998).

Inaccurate catheter placement occurs in a substantial number of cases, as frequently as 40% in some reports. There are multiple techniques and equipment available for catheter insertion. One common technique involves giving a bolus of local anesthetic to provide a surgical block followed by the introduction of a “nonstimulating” catheter (Klein et al., 2000).

However, by using this technique, it is possible to provide a successful surgical block but inaccurate catheter placement. For outpatients, this complication becomes more vexing because the inadequate perineural infusion often will not be detected until after surgical block resolution at home. Some investigators first insert the catheter and then administer a bolus of local anesthetic via the catheter in an effort to avoid this problem with a reported failure rate of 1% to 8%.
Alternatively, catheters that deliver current to their tips have been developed in an attempt to improve initial placement success rates (Boezaart et al., 1999).

These catheters provide feedback on the positional relationship of the catheter tip to the target nerve before local anesthetic dosing. Although there is some evidence that passing current via the catheter may slightly improve the accuracy of catheter placement with minor benefits in the lower extremity, it is only fair to note that the non-stimulating catheters in these three studies were advanced 4 to 10 cm past the needle tip (a choice that most likely increased the risk of excessive catheter tip-to-nerve distance and decreased the effectiveness of the local anesthetic infusion) (Capdevila et al., 2002).

Fig. (17): Site of entry
Although there are numerous catheter placement techniques reported from ultrasound guidance and fluoroscopic guidance to nerve stimulation, few studies specifically address the question of which technique is optimal for the various catheter locations. Intense interest in ultrasound-guided regional anesthesia has resulted in multiple randomized, controlled trials comparing this technique with nerve stimulation or with a combination of the two for placement of single-injection nerve blocks. However, data from these studies cannot be generalized to peri-neural catheter placement. This is because although for single injection blocks the angle between the long axis of the placement needle and nerve is relatively not important, for peri-neural catheter insertion, it is critical because the catheters tend to exit the needle and traverse past any nerve that is perpendicular to the needle itself. The perivascular approach (i.e., 3-in-1 block) to the lumbar plexus is based on the premise that injection of a large volume of local anesthetic within the femoral canal while maintaining distal pressure will result in proximal spread of solution into the psoas compartment and consequent lumbar plexus block. (Winnie et al., 1973).

However, recent imaging studies suggest that blockade occurs through lateral (lateral femoral cutaneous nerve) and medial (obturator nerve) spread of injected solution. (Marhofer et al., 2000)

Indications for femoral nerve block include anesthesia for knee arthroscopy in combination with intra-articular local anesthesia, as well as analgesia for femoral shaft fractures, anterior cruciate ligament reconstruction, and total-knee arthroplasty as a part of multimodal regimens. Their use in complex knee operations is associated with lower pain scores and fewer hospital admissions after same-day surgery. (Capdevila et al. 2005).
In most adults, 20 to 40 mL of local anesthetic will produce a successful femoral block. Due to the multiplicity and divergence of the nerve supply to the joints of the lower extremity, a femoral nerve block per se is almost never adequate as the sole anesthetic for lower limb surgery. It is almost always necessary to block the other three major peripheral nerves to the lower extremity as well. A femoral nerve block is therefore usually performed in conjunction with a sciatic, and/or obturator, and/or lateral cutaneous nerve of the thigh block. (Boezaart et al., 1999)

Investigators have added clonidine to the long-acting local anesthetic (1 to 2 μg/mL) for continuous perineural femoral, anterior lumbar plexus, interscalene, and popliteal infusions. Unfortunately, whereas clonidine increases the duration of single-injection nerve blocks, particularly those with intermediate duration agents (such as mepivacaine and lidocaine), the only controlled investigations of adding clonidine to a continuous ropivacaine infusion (μg/mL) failed to reveal any clinically relevant benefits. (Ilfeld et al., 2005).

In addition, epinephrine and opioids have been added to local anesthetic infusions, but there are insufficient data to draw any conclusions regarding these additives. Investigations of interscalene, infraclavicular, axillary, fascia iliaca, extended femoral, subgluteal, and popliteal catheters suggest that the optimal local anesthetic dosing regimen varies with anatomic location. Therefore, data from studies involving one catheter location cannot necessarily be applied to another anatomic location. Many variables probably affect the optimal regimen, including the surgical procedure, catheter location, physical therapy regimen, and the specific local anesthetic infused. It is possible that adequate analgesia for procedures inducing mild postoperative pain

would be adequately treated with a bolus-only dosing regimen. (Rawal et al., 2002).

In addition, it is possible that stimulating catheters may be placed closer to the target nerve/plexus compared with nonstimulating devices. If this proves true, then potentially different dosing regimens, basal rates, and bolus doses would be optimal for different types of catheters and also possibly for different placement techniques (e.g., nerve stimulation vs. ultrasound guidance). (Ilfeld et al., 2008).

The anterior approach to the femoral nerve is similar for “single shot” or continuous nerve blocks. This communication will outline the technique for continuous femoral nerve block only. For “single shot” block a 50 mm 22 GSstimuplex needle is typically used and the local anesthetic agent is injected after location of the nerve with the nerve stimulator set at 0.4 – 0.6 mA and 200 - 300μs.

Most continuous catheter techniques that were developed after the initial attempts of Ansbro in 1946 were hampered by inaccurate catheter placement or catheter dislodgement. (Allen et al., 1998).

In order to provide reliable analgesia for lower extremity surgery and prevent readmission due to failed catheter placement, it was necessary to develop a method to ensure real-time catheter positioning (i.e., during placement). This can now be done at insertion with all continuous peripheral nerve blocks (rather than hours later when the initial block has worn off), by stimulating the nerves via both the needle through which the catheter is placed and via the catheter itself. This accuracy of catheter placement is combined with a method to secure the catheter that prevents dislodgement. (Capdevilla et al., 1999).
The femoral nerve block is mainly indicated for the pain control associated with unilateral anterior knee surgery. It is important to note that the posterior obturator nerve gives off an articular branch that supplies the posterior aspect of the knee and this nerve may be responsible for the pain experienced in the posterior aspect of the knee following knee surgery despite an effective femoral nerve block. It was originally thought that this pain was due to the absence of a sciatic nerve block, but work done by the Virginia Mason group disputed this notion. (Capdevilla et al., 1999).

Allen and co-workers demonstrated that there was no difference in postoperative pain if a sciatic nerve block was done in conjunction with a femoral nerve block. It is, however, necessary to perform a sciatic nerve block additionally if surgery distal or posterior to the knee joint (for example anterior or posterior cruciate ligament repair) is done. It is often necessary to block the obturator and/or sciatic nerve separately in addition to the femoral nerve after total knee replacement surgery. The pain experienced in the posterior aspect of the knee is often short-lived and effectively controlled with “single-shot” blocks. (Allen et al., 1998).

Continuous femoral nerve blocks have been demonstrated to improve the outcome of total knee arthroplasty. Outcome with continuous femoral nerve block was better than “single shot” femoral block and continuous epidural anesthesia. (Capdevilla et al., 1999).

Femoral blocks are predictably successful if the needle is placed deep to the fascia iliaca. Using a nerve stimulator, this will be the case when brisk twitches of the quadriceps muscles are evoked that move the patella while being able to dial the nerve stimulator output down to between 0.3 and 0.6 mA at a pulse width of 200 - 300μs.
Another common mistake is to stimulate the nerve to the sartorius muscle, which is situated superficial to the fascia iliaca. The local anesthetic agent will then not reach the femoral nerve. Aim the bevel of the needle in the direction in which the catheter is intended to go – cephalad in this instance.

![Fig. (19): StimuCath needle](image)

The StimuCath needle is an insulated Tuohy needle with a bare tip and a bare proximal area. PNS = Peripheral Nerve Stimulator.
Fig.(20): Anatomical landmarks and needle placement
A = line marking femoral artery B = Inguinal crease C = Intended path for tunneling catheter Needle entry is 1 – 2 cm lateral of the femoral artery and aimed approximately 45° cephalad

Introduce the non-stimulating catheter into the needle. The catheter is then gradually advanced beyond the tip of the needle for a distance of approximately 3 to 5 centimeters. The catheter is now correctly placed near the femoral nerve but will most likely dislodge over time unless secured.

Penetrate the skin with the inner steel stylet of the needle 1 – 3 mm from the catheter entry site and advance the stylet subcutaneously in a lateral direction to exit the skin 8 – 10 cm laterally.
Fig. (21): Tunneling

Insert the inner stylet of the needle 2 – 3 mm from the catheter exit wound and advance subcutaneously to exit the skin 6 – 10 cm laterally.

"Rail-road” the needle over the stylet. Remove the stylet and feed the catheter retrogradely through the needle. After passage of the catheter, remove the needle and observe the skin bridge. Remove the stylet and feed the catheter retrogradely through the needle.
Insert the inner stylet of the needle 3 – 5 mm from the catheter exit site and advance subcutaneously to exit the skin approximately 8 – 10 cm laterally and “railroad the needle retrogradely back over the stylet.

After passage of the catheter, remove the needle and observe the skin bridge. Remove the needle and secure the catheter with sterile dressings. Observe the skin bridge. If the skin bridge is undesirable, allow the needle to exit through the same hole in the skin as the catheter. Be careful not to damage the catheter with the needle.
Fig. (23): Tunneling Remove the stylet from the needle and feed the proximal end of the catheter through the needle.

Fig. (24): Bridging
Fig.(23) : Injection of local anesthetic agent via the catheter. Inject the rest of the bolus dose in 5 ml increments.
Patients and Methods

This study was conducted on 100 patients of ASA physical status I-II scheduled for elective knee surgery in The University Hospital Benha Faculty of Medicine.

Exclusion criteria included:

- Patients refusing local anesthetic technique.
- ASA physical status III or IV.
- Patients with abnormal coagulation.
- Chronically on analgesic patients.
- Patients with known sensitivity to the investigating drugs.
- Dementia.
- Patients with peripheral neuropathy.
- Pregnancy.
- Infection at the site of puncture.

Patients were randomly allocated into 3 main groups Group I ,Group II and Group III as following :

**Group I :** Received general anesthesia alone (20 patients).

**Group II:** Which received combined general epidural anesthesia, a Tuohy needle with a laterally facing opening was chosen. The method used for identifying the epidural space was loss-of-resistance technique. Epidural catheters were inserted only 2 to 3 cm into the epidural space.

This group was further subdivided into 2 subgroups IIA and IIB:

**Subgroup IIA:** Epidural anesthesia was conducted using 10 ml of bupivacaine 0.25% (2.5 mg/ml solution) followed by continuous infusion at a rate of 10 ml/hour till the end of operation then postoperative boluses on request.

**Subgroup IIB:** Clonidine was added to LA solution at a dose of 1 µg/mL epidural anesthesia was conducted using 10 ml of bupivacaine0.25% (2.5
mg/ml solution)+clonidine 1 µg/mL followed by continuous infusion at a rate of 10 ml/hour) till the end of operation then postoperative boluses on request.

**Group III:** Received continuous femoral block and was further subdivided into 2 subgroups IIIA and IIIB:

**Subgroup IIIA:** Femoral anesthesia was conducted using 20 ml of bupivacaine 0.25% (2.5 mg/ml solution) followed by continuous infusion at a rate of 10 ml/hour till the end of operation then postoperative boluses on request.

**Subgroup IIIB:** Clonidine was added to LA solution at a dose of 1µg/mL femoral anesthesia was conducted using 20 ml of bupivacaine 0.25% (2.5 mg/ml solution)+clonidine 1 µg/mL followed by continuous infusion at a rate of 10 ml/hour) till the end of operation then postoperative boluses on request.

All patients was subjected to careful history taking, clinical examination and laboratory investigations. On the patient's arrival to the operating room a 18G intravenous cannula was inserted in the arm before starting the block, perioperative fluid requirements will be calculated and administered throughout the procedure, full noninvasive monitoring commenced [baseline level of consciousness, pulse oximeter, vital signs (respiratory rate, blood pressure and heart rate) and ECG]. Continuous epidural or continuous femoral block was then performed in groups II&III respectively. Balanced general anesthesia was induced in all three groups using 2ug/kg fentanyl followed by thiopental 5-7mg/kg, atracurium 0.5mg/kg as initial dose followed by top up doses. Anesthesia was maintained by isoflurane as inhalational agent.

Intraoperative data collected was: Non-invasive mean arterial blood pressure, Heart rate and MAC.
BP&HR were measured preoperative at baseline before giving general anesthesia, epidural or femoral block and then every 30 minutes after that, at 30, 60, 90 and 120 minutes.

MAC was measured after 30 minutes of induction of general anesthesia for all groups, then 30 minutes apart, at 60, 90 and 120 minutes.

Postoperative pain was assessed using visual analogue scale (VAS), Time of first request of LA bolus, number of requests per 24 hours and the total dose of local anesthetic per 24 hours. Readings was taken 2,4,8,12&24 hours postoperatively. VAS is a score for pain measurement ranging from 0 to 10 as follows: 0-2 score means no pain, 3-4 means mild pain, 5-6 moderate pain, 7-8 severe pain, 9-10 worst possible pain.

![Visual analogue scale](image)

**Fig. (26): Visual analogue scale**

All patients were visited before surgery and will be given a full explanation; informed consent will be obtained and patients will be instructed to the use of the visual analogue scale (VAS) of pain. Data collected will be statistically analyzed, P<0.05 will be considered statistically significant.
Femoral block was performed using the peripheral nerve stimulation method. PLEXÝGON nerve stimulator will be used together with insulated needles. Initial current intensity of 1.2mA was done to locate the nerve then reduction of the stimulating current to ≤0.4mA was done to confirm close proximity to the nerve.

Patient was placed the patient in supine position, then the anterior superior iliac spine and the symphysis pubis were identified, and a line between these two landmarks was drawn. This line represents the inguinal ligament. The femoral nerve passes through the center of the line, which makes this landmark useful for positioning the needle in the inguinal crease, particularly in an obese patient. Then the femoral pulse was palpated and mark it at the inguinal crease. The needle was directed cephalad toward the center of the inguinal ligament line. Needle was entered (1–1.5 cm) lateral to the artery in the inguinal crease. At this location the femoral nerve is wide and superficial, and the needle does not pass through significant muscle mass. A 16-gauge sheathed needle was advanced at that point. The nerve stimulator is initially set at 1.0 to 1.2 mA. The needle is directed cephalad at approximately a 30° to 45° angle. A brisk “patellar snap” with the current at 0.4 mA or less is indicative of successful localization of the needle near the femoral nerve. The nerve is usually superficial, rarely beyond 3 cm from the skin. The nerve stimulator was clipped to the proximal bare area of the needle and two definite “pops” are felt when the needle penetrates first the fascia lata and then the iliaca fascia. It is very important to penetrate both these layers of fascia, since the electrical current may well cross the fascia layer and cause muscle twitching, but the local anesthetic agent will not cross the fascia layer if deposited superficial to it. When the needle reaches the depth of the artery, a pulsation of the hub is visible. Commonly, the anterior branch of the femoral nerve was identified first. Stimulation of
this branch leads to contraction of the sartorius muscle on the medial aspect of the thigh and should not be accepted. The needle should be redirected slightly laterally and with a deeper direction to encounter the posterior branch of the femoral nerve. Stimulation of this branch was identified by patellar ascension as the quadriceps contracts. A 20 gauge catheter was threaded through the needle and tunneling was done. A total of 20 mL of solution was injected incrementally after negative aspiration followed by continuous infusion.

**Investigating drugs included:**

1. **Bupivacaine:** Marcaine 0.5% conc. diluted to 0.25% conc. (2.5 mg/ml solution) (Astra-Zenica).

2. **Clonidine:** Catapres ampoule 1 ml (150µg/ml) (Boehringer Ingelheim).
Fig. (27): 50mm (Left) & 100mm (Right) LOCOPLEX® insulated needles

Fig. (28): PLEXÝGON nerve stimulator
Statistical Analysis

Data were collected, presented in tables and statistically analyzed using the suitable statistical methods which include:

1) Arithmetic mean (X):

   It equals the sum of all observations divided by their number.

   \[ X = \frac{\sum X}{n} \]

   Where: \( \sum X \) = Sum of all observations.
   
   \( n \) = Number of observations.

2) Standard deviation (S.D.):

   It is calculated from the following equation:

   \[ SD = \sqrt{\frac{(X - \overline{X})^2}{n-1}} \]

   Where: \( X \) = Value of observations.
   
   \( \overline{X} \) = Mean of all observations.
   
   \( n-1 \) = Number of observations minus 1.

3) Student’s t-test (t):

   For comparison of two sample means; the following formula was used.

   \[ t = \frac{[X_1 - X_2]}{\sqrt{\frac{(SD_1)^2}{n_1} + \frac{(SD_2)^2}{n_2}}} \]

   Where:
- \( X_1 \) = Mean of sample No.1
- \( X_2 \) = Mean of sample No.2
- \( SD_1 \) = Standard deviation of sample No.1
- \( SD_2 \) = Standard deviation of sample No.2
- \( n_1 \) = number of cases in sample No.1
- \( n_2 \) = number of cases in sample No.2

4) **Chi square (\( X^2 \))**: For comparison of frequencies of more than two samples.

\[
X^2 = \sum \frac{(O - T)^2}{T}
\]

Where:
- \( \sum \) = Sum.
- \( O \) = Observed frequency.
- \( T \) = Theoretical frequency.

5) **Z test**:
   Used for comparison between percentages of two samples.

\[
Z = \frac{[P_1 - P_2]}{\sqrt{\frac{(P_1 Q_1)}{n_1} + \frac{(P_2 Q_2)}{n_2}}}
\]

Where:
- \( P_1 \) = Proportion in sample No.1
- \( P_2 \) = Proportion in sample No.2
- \( Q_1 = 1 - P_1 \)
- \( Q_2 = 1 - P_2 \)
• $n_1 =$ Number of cases in sample No.1
• $n_2 =$ Number of cases in sample No.2

6) **F test**: Used for comparison of more than two samples means and this was done using Microsoft program on IBM computer.
Results

Data were represented as mean ± SD, numbers or percentage.

- P > 0.05 non significant.
- P <0.05 significant.
- P < 0.001 highly significant.
- P < 0.0001 very highly significant.

The mean age, weight and sex ratio of the 5 groups are shown in (Table 3&4). The mean age was 33.4±11.6, 32.4±11.3, 32.4±11.7, 33.0±11.8 and 32.1±11.4 for groups I, IIA, IIB, IIIA and IIIB respectively. There was no statistically significant difference (P > 0.05) between the 5 groups. The mean weight was 84.5±12.4, 84.9±12.8, 83.3±10.8, 83.6±10.9 and 85.0±12.8 for groups I, IIA, IIB, IIIA and IIIB respectively. There was no statistically significant difference (P > 0.05) between the 5 groups. Sex ratio (Male/female) (Table 4) was 12/8, 15/5, 12/18, 12/8, 13/7 and 11/9 for groups I, IIA, IIB, IIIA and IIIB respectively. There was no statistically significant difference (P > 0.05) between the 5 groups.

Table (3): Means ± SD of ages and weight of the study groups

<table>
<thead>
<tr>
<th>Study group Variables</th>
<th>I</th>
<th>II A</th>
<th>II B</th>
<th>III A</th>
<th>III B</th>
<th>F test</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>AGE</td>
<td>33.4±11.6</td>
<td>32.4±11.3</td>
<td>32.4±11.7</td>
<td>33.0±11.8</td>
<td>32.1±11.4</td>
<td>.020</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>WT</td>
<td>84.5±12.4</td>
<td>84.9±12.8</td>
<td>83.3±10.8</td>
<td>83.6±10.9</td>
<td>85.0±12.8</td>
<td>.082</td>
<td>&gt;0.05</td>
</tr>
</tbody>
</table>

Table (4): Sex distribution of the study groups
### Intra-operative data

1. **Minimal Alveolar Concentration (MAC)**

   MAC at 30 minutes, 60 minutes, 90 minutes, and 120 minutes later was recorded for the 5 groups as shown in (Table-5). **MAC at 30 min** was 1.44±0.1, 0.65±0.11, 0.67±0.13, 0.68±0.05 and 0.77±0.07. **MAC at 60 min** was 1.42±0.12, 0.65±0.12, 0.63±0.13, 0.69±0.07 and 0.67±0.085. **MAC at 90 min** was 1.42±0.1, 0.64±0.1, 0.64±0.13, 0.72±0.05 and 0.65±0.3. **MAC at 120 min** was 1.46±0.1, 0.63±0.1, 0.7±0.2, 0.73±0.07 and 0.69±0.08 for groups I, IIA, IIB, IIIA and IIIB respectively.

**Table (5) Mean± SD of intra-operative MAC values at different times of the study groups**
P <0.001 in comparing any group to group (I). There was statistically significant difference in means of MAC between all groups and the control group (general group).

Table (6): Mean± SD of intra-operative MAC values of group II A and II B

<table>
<thead>
<tr>
<th>Study group</th>
<th>Variables</th>
<th>II A</th>
<th>II B</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MAC 30min</td>
<td>0.65±0.11</td>
<td>0.67±0.13</td>
</tr>
<tr>
<td></td>
<td>MAC 60min</td>
<td>0.65±0.13</td>
<td>0.63±0.13</td>
</tr>
<tr>
<td></td>
<td>MAC 90min</td>
<td>0.64±0.11</td>
<td>0.64±0.13</td>
</tr>
<tr>
<td></td>
<td>MAC 120min</td>
<td>0.63±0.11</td>
<td>0.7±0.19</td>
</tr>
</tbody>
</table>

P> 0.05 there was no statistically significant difference between the two groups (IIA&IIB) in MAC at different readings

Table (7): Mean± SD of intra-operative MAC values of group II A and III A
P> 0.05 there was no statistically significant difference between the two groups (IIA&IIIA) in MAC at different readings

**Table (8): Mean± SD of intra-operative MAC values of group II B and III B**

<table>
<thead>
<tr>
<th>Study group</th>
<th>II B</th>
<th>III B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Variables</td>
<td>N=20</td>
<td>N=20</td>
</tr>
<tr>
<td></td>
<td>X±SD</td>
<td>X±SD</td>
</tr>
<tr>
<td>MAC30 min</td>
<td>0.67±0.134</td>
<td>0.77±0.07</td>
</tr>
<tr>
<td>MAC60 min</td>
<td>0.63±0.126</td>
<td>0.67±0.085</td>
</tr>
<tr>
<td>MAC90 min</td>
<td>0.64±0.131</td>
<td>0.65±0.3</td>
</tr>
<tr>
<td>MAC120 min</td>
<td>0.70±0.195</td>
<td>0.69±0.08</td>
</tr>
</tbody>
</table>

P> 0.05 there was no statistically significant difference between the two groups (IIB&IIIB) in MAC at different readings

**Table (9): Mean± SD of intra-operative MAC values of group IIIA and IIIB**
<table>
<thead>
<tr>
<th>Study group Variables</th>
<th>III A N=20</th>
<th>III B N=20</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>X±SD</td>
<td>X±SD</td>
</tr>
<tr>
<td>MAC 30min</td>
<td>0.68±0.05</td>
<td>0.77±0.07</td>
</tr>
<tr>
<td>MAC 60min</td>
<td>0.69±0.07</td>
<td>0.67±0.085</td>
</tr>
<tr>
<td>MAC 90min</td>
<td>0.72±0.05</td>
<td>0.65±0.3</td>
</tr>
<tr>
<td>MAC 120min</td>
<td>0.73±0.07</td>
<td>0.69±0.08</td>
</tr>
</tbody>
</table>

P> 0.05 there was no statistically significant difference between the two groups (IIIA&IIIB) in MAC at different readings

**2-Blood Pressure (BP)**

BP at baseline, 30 minutes, 60 minutes, 90 minutes, and 120 minutes later was recorded for the 5 groups as shown in (Table-10). The mean BP:
At baseline was 92.5±1.9, 91.6±7.1, 90.1±4.9, 91.4± 4.7 and 90.6±4.5. BP at 30 min was 92.6±1.9, 73.1±8.4, 66. 1±6.8, 77.8± 5.1 and 75.9±5.6. BP at 60 min was 93.2±1.7, 74.9±6.6, 70.7±4.7, 77.9± 4.1 and 74.8±6.3. BP at 90 min was 93.5±1.8, 75.5±7.5, 71.3±5.1, 78.7± 5.4 and 73.2±6.5. BP at 120 min was 93.2±1.5, 76.5±6.6, 70.6±5.1, 78.2± 4.7 and 72.5±8.3 for groups I, IIA, IIB, IIIA and IIIB respectively.

Table (10) Mean± SD of intra-operative Mean BP values at different times of the study groups

<table>
<thead>
<tr>
<th>Study group Variables</th>
<th>I</th>
<th>II A</th>
<th>II B</th>
<th>III A</th>
<th>III B</th>
</tr>
</thead>
<tbody>
<tr>
<td>BP at baseline</td>
<td>92.5±1.9</td>
<td>91.6±7.1</td>
<td>90.1±4.9</td>
<td>91.4±4.7</td>
<td>90.6±4.5</td>
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<tr>
<td>BP 30 min</td>
<td>92.6±1.9</td>
<td>73.1±8.4</td>
<td>66.1±6.8</td>
<td>77.8±5.1</td>
<td>75.9±5.6</td>
</tr>
<tr>
<td>BP 60 min</td>
<td>93.2±1.7</td>
<td>74.9±6.6</td>
<td>70.7±4.7</td>
<td>77.9±4.1</td>
<td>74.8±6.3</td>
</tr>
<tr>
<td>BP 90 min</td>
<td>93.5±1.8</td>
<td>75.5±7.5</td>
<td>71.3±5.1</td>
<td>78.7±5.4</td>
<td>73.2±6.5</td>
</tr>
<tr>
<td>BP 120 min</td>
<td>93.2±1.5</td>
<td>76.5±6.6</td>
<td>70.6±5.1</td>
<td>78.2±4.7</td>
<td>72.5±8.3</td>
</tr>
</tbody>
</table>

P <0.001 in comparing any group to group (I). There was statistically significant difference in means of BP between all groups and the control group (general group).
Table (11) Mean± SD of intra-operative mean BP values of group II A and II B

<table>
<thead>
<tr>
<th>Study group Variables</th>
<th>II A N=20 X±SD</th>
<th>II B N=20 X±SD</th>
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<tbody>
<tr>
<td>BP baseline</td>
<td>91.6±7.1</td>
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</tr>
<tr>
<td>BP 30min</td>
<td>73.1±8.4</td>
<td>66.1±6.8</td>
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<tr>
<td>BP 60min</td>
<td>74.9±6.6</td>
<td>70.7±4.7</td>
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<td>BP 90min</td>
<td>75.5±7.5</td>
<td>71.3±5.1</td>
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<tr>
<td>BP 120min</td>
<td>76.5±6.6</td>
<td>70.6±5.1</td>
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</table>

P> 0.05 there was no statistically significant difference between the two groups (IIA&IIB) in BP at different readings.

Table (12) Mean± SD of intra-operative Mean BP values of group II A and III A

<table>
<thead>
<tr>
<th>Study group Variables</th>
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<tbody>
<tr>
<td>BP baseline</td>
<td>91.6±7.1</td>
<td>91.4±4.7</td>
</tr>
<tr>
<td>BP 30min</td>
<td>73.1±8.4</td>
<td>77.8±5.1</td>
</tr>
<tr>
<td>BP 60min</td>
<td>74.9±6.6</td>
<td>77.9±4.1</td>
</tr>
<tr>
<td>BP 90min</td>
<td>75.5±7.5</td>
<td>78.7±5.4</td>
</tr>
<tr>
<td>BP 120min</td>
<td>76.5±6.6</td>
<td>78.2±4.7</td>
</tr>
</tbody>
</table>

P> 0.05 there was no statistically significant difference between the two groups (IIA&IIIA) in BP at different readings.

Table (13) Mean± SD of intra-operative Mean BP values of group II A and III A
P> 0.05 there was no statistically significant difference between the two epidural groups (IIB&IIIB) in BP at different readings

<table>
<thead>
<tr>
<th>Study group</th>
<th>Variables</th>
<th>II B</th>
<th>III B</th>
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</thead>
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<td>N=20</td>
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<tr>
<td>BP baseline</td>
<td>90.1±4.9</td>
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<td>90.6±4.5</td>
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<td>BP 30min</td>
<td>66.1±6.8</td>
<td></td>
<td>75.9±5.6</td>
</tr>
<tr>
<td>BP 60min</td>
<td>70.7±4.7</td>
<td></td>
<td>74.8±6.3</td>
</tr>
<tr>
<td>BP 90min</td>
<td>71.3±5.1</td>
<td></td>
<td>73.2±6.5</td>
</tr>
<tr>
<td>BP 120min</td>
<td>70.6±5.1</td>
<td></td>
<td>72.5±8.3</td>
</tr>
</tbody>
</table>

Table (14) Mean± SD of intra-operative Mean BP values of group III A and III B

<table>
<thead>
<tr>
<th>Study group</th>
<th>Variables</th>
<th>III A</th>
<th>III B</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=20</td>
<td>X±SD</td>
<td>N=20</td>
</tr>
<tr>
<td>BP baseline</td>
<td>91.4±4.7</td>
<td></td>
<td>90.6±4.5</td>
</tr>
<tr>
<td>BP 30min</td>
<td>77.8±5.1</td>
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<td>75.9±5.6</td>
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<tr>
<td>BP 60min</td>
<td>77.9±4.1</td>
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<td>74.8±6.3</td>
</tr>
<tr>
<td>BP 90min</td>
<td>78.7±5.4</td>
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<td>73.2±6.5</td>
</tr>
<tr>
<td>BP 120min</td>
<td>78.2±4.7</td>
<td></td>
<td>72.5±8.3</td>
</tr>
</tbody>
</table>

P> 0.05 there was no statistically significant difference between the two groups (IIIA&IIIB) in BP at different readings
3-Heart Rate (HR)

HR at baseline, 30 minutes, 60 minutes, 90 minutes, and 120 minutes later was recorded for the 5 groups as shown in (Table 15). The mean HR; *At baseline* was 83.2±2.3, 84.2±4.3, 86.1±4.4, 86.7±3.6 and 86.6±4.5. HR *at 30 min* was 80.4±3.9, 69.9±5.9, 66.7±2.8, 72.8±5.1 and 70.9±5.6. HR *at 60 min* was 81.3±5.1, 68.7±3.9, 67.1±3.7, 70.9±4.1 and 68.8±6.3. HR *at 90 min* was 82.4±7.7, 67.2±7.8, 65.7±5.5, 69.7±5.4 and 68.8±7.6. HR *at 120 min* was 80.4±2.3, 69.5±6, 68.7±6.6, 71.2±4.7 and 69.5±8.3 for groups I, IIA, IIB, IIIA and IIIB respectively.

**Table (15): Mean± SD of intra-operative HR values at different times of the study groups**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Study group</th>
<th>I</th>
<th>II A</th>
<th>II B</th>
<th>III A</th>
<th>III B</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR at baseline</td>
<td>83.2±2.3</td>
<td>84.2±4.3</td>
<td>86.1±4.4</td>
<td>86.7±3.6</td>
<td>86.6±4.5</td>
<td></td>
</tr>
<tr>
<td>HR 30min</td>
<td>80.4±3.9</td>
<td>69.9±5.9</td>
<td>66.7±2.8</td>
<td>72.8±5.1</td>
<td>70.9±5.6</td>
<td></td>
</tr>
<tr>
<td>HR 60min</td>
<td>81.3±5.1</td>
<td>68.7±3.9</td>
<td>67.1±3.7</td>
<td>70.9±4.1</td>
<td>68.8±6.3</td>
<td></td>
</tr>
<tr>
<td>HR 90min</td>
<td>82.4±7.7</td>
<td>67.2±7.8</td>
<td>65.7±5.5</td>
<td>69.7±5.4</td>
<td>68.8±7.6</td>
<td></td>
</tr>
</tbody>
</table>
HR 120min | 80.4±1.3 | 69.5±6 | 68.7±6.6 | 71.2±4.7 | 69.5±8.3

Figure (31) Mean of HR at different times of the study groups

P <0.001 in comparing any group to group (I). There was statistically significant difference in means of HR between all groups and the control group (general group).

Table (16): Mean± SD of intra-operative HR values of group II A and IIB

<table>
<thead>
<tr>
<th>Study group</th>
<th>Variables</th>
<th>II A N=20</th>
<th>II B N=20</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>X±SD</td>
<td>X±SD</td>
<td>X±SD</td>
</tr>
<tr>
<td>HR baseline</td>
<td>84.2±4.3</td>
<td>86.1±4.4</td>
<td></td>
</tr>
<tr>
<td>HR 30min</td>
<td>69.9±5.9</td>
<td>66.7±2.8</td>
<td></td>
</tr>
<tr>
<td>HR 60min</td>
<td>68.7±3.9</td>
<td>67.1±3.7</td>
<td></td>
</tr>
<tr>
<td>HR 90min</td>
<td>67.2±7.8</td>
<td>65.7±5.5</td>
<td></td>
</tr>
<tr>
<td>HR 120min</td>
<td>69.5±6</td>
<td>68.7±6.6</td>
<td></td>
</tr>
</tbody>
</table>

P > 0.05 there was no statistically significant difference between the two groups (IIA&IIB) in HR at different readings.
Table (17) Mean± SD of intra-operative HR values of group II A and III A

<table>
<thead>
<tr>
<th>Study group Variables</th>
<th>II A N=20</th>
<th>III A N=20</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>X±SD</td>
<td>X±SD</td>
</tr>
<tr>
<td>HR baseline</td>
<td>84.2±4.3</td>
<td>86.7±3.6</td>
</tr>
<tr>
<td>HR 30min</td>
<td>69.9±5.9</td>
<td>72.8±5.1</td>
</tr>
<tr>
<td>HR 60min</td>
<td>68.7±3.9</td>
<td>70.9±4.1</td>
</tr>
<tr>
<td>HR 90min</td>
<td>67.2±7.8</td>
<td>69.7±5.4</td>
</tr>
<tr>
<td>HR 120min</td>
<td>69.5±6</td>
<td>71.2±4.7</td>
</tr>
</tbody>
</table>

P> 0.05 there was no statistically significant difference between the two groups (IIA&IIIA) in HR at different readings.

Table (18): Mean± SD of intra-operative HR values of group II B and IIIB

<table>
<thead>
<tr>
<th>Study group Variables</th>
<th>II B N=20</th>
<th>III B N=20</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>X±SD</td>
<td>X±SD</td>
</tr>
<tr>
<td>HR baseline</td>
<td>86.1±4.4</td>
<td>86.6±4.5</td>
</tr>
<tr>
<td>HR 30min</td>
<td>66.7±2.8</td>
<td>70.9±5.6</td>
</tr>
<tr>
<td>HR 60min</td>
<td>67.1±3.7</td>
<td>68.8±6.3</td>
</tr>
<tr>
<td>HR 90min</td>
<td>65.7±5.5</td>
<td>68.8±7.6</td>
</tr>
<tr>
<td>HR 120min</td>
<td>68.7±6.6</td>
<td>69.5±8.3</td>
</tr>
</tbody>
</table>

P> 0.05 there was no statistically significant difference between the two groups (IIB&IIIB) in HR at different readings.

Table (19): Mean± SD of intra-operative HR values of group III A and IIIB
<table>
<thead>
<tr>
<th>Study group Variables</th>
<th>III A N=20</th>
<th>III B N=20</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>X±SD</td>
<td>X±SD</td>
</tr>
<tr>
<td>HR baseline</td>
<td>86.7±3.6</td>
<td>86.6±4.5</td>
</tr>
<tr>
<td>HR 30min</td>
<td>72.8±5.1</td>
<td>70.9±5.6</td>
</tr>
<tr>
<td>HR 60min</td>
<td>70.9±4.1</td>
<td>68.8±6.3</td>
</tr>
<tr>
<td>HR 90min</td>
<td>69.7±5.4</td>
<td>68.8±7.6</td>
</tr>
<tr>
<td>HR 120min</td>
<td>71.2±4.7</td>
<td>69.5±8.3</td>
</tr>
</tbody>
</table>

P> 0.05 there was no statistically significant difference between the two groups (IIIA&IIIB) in HR at different readings.

Post-operative data

1-Visual Analogue Scale (VAS)
VAS after 2 hours of recovery, 4 hours, 8 hours, 12 hours and 24 later was recorded for the 5 groups as shown in (Table-20). The mean VAS at 2 hours was 4.05±1.1, 3.45±0.51, 2.55±0.68, 3.5±0.51, 2.45±0.51 and VAS at 4 hours was 4.95±1.22, 3.6±0.68, 2.5±0.51, 3.65±0.58 and 2.6±1.05 VAS at 8 hours was 4.8±1.05, 3.3±0.73, 2.65±0.74, 3.2±1.5 and 2.8±0.89 VAS at 12 hours was 4.6±1.5, 3.5±0.82, 2.75±0.78, 3.75±1.55 and 2.65±1.39 VAS at 24 hours was 4.4±0.94, 3.95±0.82, 2.6±0.68, 3.65±1.35 and 2.8±1.46 for groups I, IIA, IIB, IIIA and IIIB respectively.

**Table (20): Mean± SD of Post-operative VAS values of the study groups**

<table>
<thead>
<tr>
<th>Study group</th>
<th>I</th>
<th>II A</th>
<th>II B</th>
<th>III A</th>
<th>III B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Variables</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VAS after 2 hours</td>
<td>4.05±1.1</td>
<td>3.45±0.51</td>
<td>2.55±0.68</td>
<td>3.5±0.51</td>
<td>2.45±0.51</td>
</tr>
<tr>
<td>VAS 4 hours</td>
<td>4.95±1.22</td>
<td>3.6±0.68</td>
<td>2.5±0.51</td>
<td>3.65±0.58</td>
<td>2.6±1.05</td>
</tr>
<tr>
<td>VAS 8 hours</td>
<td>4.8±1.05</td>
<td>3.3±0.73</td>
<td>2.65±0.74</td>
<td>3.2±1.5</td>
<td>2.8±0.89</td>
</tr>
<tr>
<td>VAS 12 hours</td>
<td>4.6±1.5</td>
<td>3.5±0.82</td>
<td>2.75±0.78</td>
<td>3.75±1.55</td>
<td>2.65±1.39</td>
</tr>
<tr>
<td>VAS 24 hours</td>
<td>4.4±0.94</td>
<td>3.95±0.82</td>
<td>2.6±0.68</td>
<td>3.65±1.35</td>
<td>2.8±1.46</td>
</tr>
</tbody>
</table>
Figure (32): Means of VAS at different times of the study groups

There was statistically significant difference between group I and the other 4 groups P < 0.001, also there was statistically significant difference between groups with clonidine (group IIB&IIIB) and those with bupivacaine only (group IIA& group IIIA) , VAS was less in groups with clonidine additive.

Table (21): Mean± SD of Post-operative VAS values of group II A and II B

<table>
<thead>
<tr>
<th>Study group</th>
<th>II A N=20</th>
<th>II B N=20</th>
</tr>
</thead>
<tbody>
<tr>
<td>Variables</td>
<td>X±SD</td>
<td>X±SD</td>
</tr>
<tr>
<td>VAS after 2hrs</td>
<td>3.45±0.51</td>
<td>2.55±0.68</td>
</tr>
<tr>
<td>VAS4hrs</td>
<td>3.6±0.68</td>
<td>2.5±0.51</td>
</tr>
<tr>
<td>VAS8hrs</td>
<td>3.3±0.73</td>
<td>2.65±0.74</td>
</tr>
<tr>
<td>VAS12hrs</td>
<td>3.5±0.82</td>
<td>2.75±0.78</td>
</tr>
<tr>
<td>VAS24hrs</td>
<td>3.95±0.82</td>
<td>2.6±0.88</td>
</tr>
</tbody>
</table>

P<0.001 there was significant difference between the two groups (IIA&IIB) in VAS at different times.

Table (22): Mean± SD of Post-operative VAS values of group II A and III A

<table>
<thead>
<tr>
<th>Study group</th>
<th>II A N=20</th>
<th>III A N=20</th>
</tr>
</thead>
<tbody>
<tr>
<td>Variables</td>
<td>X±SD</td>
<td>X±SD</td>
</tr>
<tr>
<td>VAS after 2hrs</td>
<td>3.45±0.51</td>
<td>3.5±0.51</td>
</tr>
<tr>
<td>VAS4hrs</td>
<td>3.6±0.68</td>
<td>3.65±0.58</td>
</tr>
<tr>
<td>VAS8hrs</td>
<td>3.3±0.73</td>
<td>3.2±1.5</td>
</tr>
<tr>
<td>VAS12hrs</td>
<td>3.5±0.82</td>
<td>3.75±1.55</td>
</tr>
<tr>
<td>VAS24hrs</td>
<td>3.95±0.82</td>
<td>3.65±1.35</td>
</tr>
</tbody>
</table>

P>0.05 there was no significant difference between the two groups (IIA&IIIA) in VAS at different times.
Table (23): Mean± SD of Post-operative VAS values of group II B and III B

<table>
<thead>
<tr>
<th>Study group</th>
<th>Variables</th>
<th>II B</th>
<th>III B</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>N=20</td>
<td>N=20</td>
</tr>
<tr>
<td></td>
<td>X±SD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>VAS after 2hrs</td>
<td>2.55±0.68</td>
<td>2.45±0.51</td>
<td></td>
</tr>
<tr>
<td>VAS4hrs</td>
<td>2.5±0.51</td>
<td>2.6±1.05</td>
<td></td>
</tr>
<tr>
<td>VAS8hrs</td>
<td>2.65±0.74</td>
<td>2.8±0.89</td>
<td></td>
</tr>
<tr>
<td>VAS12hrs</td>
<td>2.75±0.78</td>
<td>2.65±1.39</td>
<td></td>
</tr>
<tr>
<td>VAS24hrs</td>
<td>2.6±0.88</td>
<td>2.8±1.46</td>
<td></td>
</tr>
</tbody>
</table>

P>0.05 there was no significant difference between the two groups (IIB&IIIB) in VAS at different times.

Table (24): Mean± SD of Post-operative VAS values of group III A and III B

<table>
<thead>
<tr>
<th>Study-group</th>
<th>Variables</th>
<th>III A</th>
<th>III B</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>N=20</td>
<td>N=20</td>
</tr>
<tr>
<td></td>
<td>X±SD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>VAS after 2hrs</td>
<td>3.5±0.51</td>
<td>2.45±0.51</td>
<td></td>
</tr>
<tr>
<td>VAS4hrs</td>
<td>3.65±0.58</td>
<td>2.6±1.05</td>
<td></td>
</tr>
<tr>
<td>VAS8hrs</td>
<td>3.2±1.5</td>
<td>2.8±0.89</td>
<td></td>
</tr>
<tr>
<td>VAS12hrs</td>
<td>3.75±1.55</td>
<td>2.65±1.39</td>
<td></td>
</tr>
<tr>
<td>VAS24hrs</td>
<td>3.65±1.35</td>
<td>2.8±1.46</td>
<td></td>
</tr>
</tbody>
</table>

P<0.001 there was significant difference between the two groups (IIIA&IIIB) in VAS at different times.
2-Time of first request for analgesia (from end of the operation)

The mean time of 1st request for systemic IV analgesia (50 mg pethidine) or LA bolus was 0.5±0.25, 3.15±0.35, 6.8±0.77, 3.45±0.51 and 6.95±0.76 for groups I, IIA, IIB, IIIA and IIIB respectively. There was statistically significant difference between group I and the other 4 groups P < 0.001, also there was statistically significant difference between groups with clonidine (group IIB&IIIB) and those with bupivacaine only (group IIA& group IIIA), first request for analgesia was delayed in groups with clonidine additive.

Table (25): Mean± SD of time of first request, number of requests/24hrs & total dose/24 hours of the study groups

<table>
<thead>
<tr>
<th>Study group Variables</th>
<th>I</th>
<th>IIA</th>
<th>IIB</th>
<th>IIIA</th>
<th>IIIIB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time of 1st request for analgesia</td>
<td>0.5±0.25</td>
<td>3.15±0.35</td>
<td>6.8±0.77</td>
<td>3.45±0.51</td>
<td>6.95±0.76</td>
</tr>
<tr>
<td>Number of requests/24hrs</td>
<td>-</td>
<td>3.55±0.6</td>
<td>2.45±0.51</td>
<td>3.6±0.5</td>
<td>2.5±0.5</td>
</tr>
<tr>
<td>Total dose of LA/24hrs</td>
<td>-</td>
<td>163.7±15.1</td>
<td>136.2±12.7</td>
<td>166.2±12.76</td>
<td>135±12.6</td>
</tr>
</tbody>
</table>

There was statistically significant difference between group I and the other 4 groups in comparing time of first request for analgesia P < 0.001
3-Number of requests for LA boluses per 24 hours

The mean number of requests for LA bolus /24 hours was 3.55±0.6, 2.45±.51, 3.6±0.5 and 2.5±0.5 for groups IIA, IIB, IIIA and IIIB respectively. There was statistically significant difference between groups with clonidine (group IIB&IIIB) and those with bupivacaine only (group IIA& group IIIA) P < 0.001, number of requests/24 was less with clonidine additive.
4-Total dose of local anesthetic per 24 hours

The mean total dose of LA (mg)/24hrs was 163.7±15.1, 136.2±12.7, 166.2±12.76 and 135±12.6 for groups IIA, IIB, IIIA and IIIB respectively. There was statistically significant difference between groups with clonidine (group IIB&IIIB) and those with bupivacaine only (group IIA& group IIIA) P < 0.001, total dose of local anesthetic/24 hours was less with clonidine additive.
**Figure (35): Means of total dose of LA (mg/24hrs) of the study groups**

**Table (26): Mean± SD of time of first request, number of requests/24& total dose /24 hours between groups IIA & IIB**

<table>
<thead>
<tr>
<th>Study group</th>
<th>Variables</th>
<th>II A</th>
<th>II B</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=20</td>
<td>X±SD</td>
<td>X±SD</td>
</tr>
<tr>
<td>Time of 1st request for analgesia</td>
<td>3.15±0.35</td>
<td>6.8±0.77</td>
<td></td>
</tr>
<tr>
<td>Number of requests/24hrs</td>
<td>3.55±0.6</td>
<td>2.45±0.51</td>
<td></td>
</tr>
<tr>
<td>Total dose of LA/24hrs</td>
<td>163.7±15.1</td>
<td>136.2±12.7</td>
<td></td>
</tr>
</tbody>
</table>

There was statistically significant difference between group IIA and group IIB (P < 0.001)
Table (27): Mean± SD of time of first request, number of requests/24& total dose /24 hours between groups IIA & IIIA

<table>
<thead>
<tr>
<th>Study group</th>
<th>Variables</th>
<th>II A</th>
<th>III A</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=20</td>
<td>N=20</td>
<td></td>
</tr>
<tr>
<td></td>
<td>X±±SD</td>
<td>X±±SD</td>
<td></td>
</tr>
<tr>
<td>Time of 1st request for LA bolus</td>
<td>3.15±0.35</td>
<td>3.45±0.51</td>
<td></td>
</tr>
<tr>
<td>Number of requests/24hrs</td>
<td>3.55±0.6</td>
<td>3.6±0.5</td>
<td></td>
</tr>
<tr>
<td>Total dose of LA/24hrs</td>
<td>163.7±15.1</td>
<td>166.2±12.76</td>
<td></td>
</tr>
</tbody>
</table>

There was no statistically significant difference between group IIA and group IIIA (P>0.05)

Table (28): Mean± SD of time of first request, number of requests/24& total dose /24 hours between groups IIB & IIIB

<table>
<thead>
<tr>
<th>Study group</th>
<th>Variables</th>
<th>II B</th>
<th>III B</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=20</td>
<td>N=20</td>
<td></td>
</tr>
<tr>
<td></td>
<td>X±±SD</td>
<td>X±±SD</td>
<td></td>
</tr>
<tr>
<td>Time of 1st request for LA bolus</td>
<td>6.8±0.77</td>
<td>6.95±0.76</td>
<td></td>
</tr>
<tr>
<td>Number of requests/24hrs</td>
<td>2.45±0.51</td>
<td>2.5±0.5</td>
<td></td>
</tr>
<tr>
<td>Total dose of LA/24hrs</td>
<td>136.2±12.7</td>
<td>135±12.6</td>
<td></td>
</tr>
</tbody>
</table>
There was no statistically significant difference between group IIB and group IIIB (P>0.05)

Table (29): Mean± SD of time of first request, number of requests/24& total dose /24 hours between groups IIIA & IIIB

<table>
<thead>
<tr>
<th>Study group</th>
<th>Variables</th>
<th>III A</th>
<th>III B</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=20</td>
<td>3.45±0.51</td>
<td>6.95±0.76</td>
</tr>
<tr>
<td></td>
<td>X±SD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time of 1st request for LA bolus</td>
<td>3.6±0.5</td>
<td>2.5±0.5</td>
<td></td>
</tr>
<tr>
<td>Number of requests/24hrs</td>
<td>166.2±12.76</td>
<td>135±12.6</td>
<td></td>
</tr>
<tr>
<td>Total dose of LA/24hrs</td>
<td></td>
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</table>

There was statistically significant difference between group IIIA and group IIIB (P < 0.001)

**DISCUSSION**

In our study 100 patients of ASA physical status I-II underwent elective knee surgery in The University Hospital of Benha Faculty of Medicine.

Patients were randomly allocated into 3 main groups Group I, Group II and Group III as following:
Group I: Received general anesthesia alone (20 patients). Group II: Which received combined general epidural anesthesia. Epidural catheters were inserted only 2 to 3 cm into the epidural space. This group was further subdivided into 2 subgroups IIA and IIB:

Subgroup IIA: Epidural anesthesia was conducted using 10 ml of bupivacaine 0.25% (2.5 mg/ml solution) followed by continuous infusion at a rate of 10 ml/hour till the end of operation then postoperative boluses on request.

Subgroup IIB: Clonidine was added to LA solution at a dose of 1 µg/mL epidural anesthesia was conducted using 10 ml of bupivacaine 0.25% (2.5 mg/ml solution) +clonidine 1 µg/mL followed by continuous infusion at a rate of 10 ml/hour) till the end of operation then postoperative boluses on request.

Group III: Received continuous femoral block and was further subdivided into 2 subgroups IIIA and IIIB:

Subgroup IIIA: Femoral anesthesia was conducted using 20 ml of bupivacaine 0.25% (2.5 mg/ml solution) followed by continuous infusion at a rate of 10 ml/hour till the end of operation then postoperative boluses on request.

Subgroup IIIB: Clonidine was added to LA solution at a dose of 1 µg/mL femoral anesthesia was conducted using 20 ml of bupivacaine 0.25% (2.5 mg/ml solution) +clonidine 1 µg/mL followed by continuous infusion at a rate of 10 ml/hour) till the end of operation then postoperative boluses on request.

Intraoperative data collected was: Non-invasive mean arterial blood pressure, Heart rate and MAC.
BP&HR were measured preoperative at baseline before giving general anesthesia, epidural or femoral block and then every 30 minutes after that, at 30, 60, 90 and 120 minutes.

MAC was measured after 30 minutes of induction of general anesthesia for all groups, then 30 minutes apart, at 60, 90, and 120 minutes.

Postoperative pain was assessed using visual analogue scale (VAS), Time of first request of LA bolus, number of requests per 24 hours and the total dose of local anesthetic per 24 hours. Readings was taken 2, 4, 8, 12, & 24 hours postoperatively. VAS is a score for pain measurement ranging from 0 to 10 as follows: 0-2 score means no pain, 3-4 means mild pain, 5-6 moderate pain, 7-8 severe pain, 9-10 worst possible pain.

As regards MAC in this study, there was statistically significant difference between the control group (general group) and the other 4 groups, p<0.001, as MAC was much lower in combined general epidural groups & combined general femoral groups than in general only group (control group). This means that epidural & femoral anesthesia provides much more decrease in consumption of general anesthetic with decrease of their side effects.

As regards BP & HR in this study, there was statistically significant difference between the control group (general group) and the other 4 groups, p<0.001, as BP & HR were much lower in combined general epidural groups & combined general femoral groups than in general only group (control group). There was no was statistically significant difference, p>0.05 between groups with clonidine and those without clonidine.
This means that epidural anesthesia provides much more decrease in BP&HR because of sympathectomy accompanying neuroaxial blocks, while the decrease in BP&HR in the femoral groups more than the general group is due to analgesic effect of the block, addition of clonidine to LA did not produce more hypotension because we used small doses.

The results of the present study agree with the results of Greene (1981) that the cardiovascular effects of neuraxial blocks are similar in some ways to the combined use of intravenous $\alpha_1$- and $\beta$-adrenergic blockers: decreased heart rate and arterial blood pressure. The sympathectomy that accompanies the techniques depends on the height of the block, with the sympathectomy typically described as extending for two to six dermatomes above the sensory level with spinal anesthesia and at the same level with epidural anesthesia.

Rooke et al (1997) agree with us that this sympathectomy causes venous and arterial vasodilation, but because of the large amount of blood in the venous system (approximately 75% of the total volume of blood), the venodilation effect predominates as a result of the limited amount of smooth muscle in venules; in contrast, the vascular smooth muscle on the arterial side of the circulation retains a considerable degree of autonomous tone. After neuraxial block–induced sympathectomy, if normal cardiac output is maintained, total peripheral resistance should decrease only 15% to 18% in normovolemic healthy patients, even with nearly total sympathectomy. In elderly patients with cardiac disease, systemic vascular resistance may decrease almost 25% after spinal anesthesia, whereas cardiac output decreases only 10%.

Greene (1981) agree with us that the heart rate during a high neuraxial block typically decreases as a result of blockade of the cardioaccelerator fibers arising from T1 to T4. The heart rate may
decrease because of a fall in right atrial filling, which decreases outflow from intrinsic chronotropic stretch receptors located in the right atrium and great veins.

As regards VAS in this study there was statistically significant difference between the control group (general group) and the other 4 groups \( p<0.001 \), as there was a great difference between the general group (much higher pain scores) and both combined epidural and combined femoral groups (much lower pain scores), also there was statistically significant difference between groups with additive (clonidine) namely group IIB & IIIB (lower VAS) and groups without clonidine namely group IIA & IIIA (higher VAS) and there was no significant difference between epidural and femoral groups.

The results of the present study agree with the results of Wheatley et al (2001) that analgesia delivered through an indwelling epidural catheter is a safe and effective method for management of acute postoperative pain. Postoperative epidural analgesia can provide analgesia superior to that with systemic opioids. Of note, however, epidural analgesia is not a generic term but incorporates a wide range of options, including the choice and dose of analgesic agents, location of catheter placement, and onset and duration of perioperative use.

Handley et al (1997) agree with us that intraoperative use of the epidural catheter as part of a combined epidural-general anesthetic technique results in less pain and faster patient recovery immediately after surgery than general anesthesia followed by systemic opioids does. Each of these options may affect the quality of postoperative analgesia, patient-reported outcomes, and even rates of morbidity and mortality.
*FY Ng et al (2012)* agree with us that multimodal pain management tackles different pain pathways: local, peripheral nerve, spinal, and central. Preoperative patient education, clarification of expectation, and discussion about different options of pain control can alleviate patient anxiety. Pre-emptive and postoperative oral analgesia with opioids and anti-inflammatory medications, intra-operative multimodal intra-articular injections, postoperative parenteral opioids, continuous epidural analgesia or continuous femoral nerve block tackle the pain pathways.

*Hirst et al (2008)* agree with us that Continuous infusion of local anesthetics via a femoral catheter provides effective pain control and reduces opioid consumption.

The results of the present study agree with the results of *Soto Mesa et al (2011)* that the use of peripheral nerve block is accepted practice for analgesia after knee replacement surgery. Continuous femoral block is a valid alternative, decreasing the use of rescue opiates and pain intensity (particularly at 48h) compared to isolated femoral block.

*Capdevila et al (1999)* agree with us that good analgesia may be associated with better outcome after total knee replacement. Lumbar epidural analgesia is perhaps the most frequently used regional technique for major lower limb arthroplasty in the UK, but its benefits must be balanced against potential adverse effects.

*Davies et al (2004)* agree with us that there is currently great interest in the use of peripheral nerve blocks but controversy remains over the ideal technique. Continuous or bolus femoral nerve block is popular but may be associated with prolonged and excessive nerve block preventing early mobilization. Additional single-shot sciatic nerve block
may be necessary for optimizing analgesia but continuous block may delay mobilization.

_Campell et al (2008)_ agree with us that postoperative regional analgesia for total knee replacement can provide excellent pain control and speedy rehabilitation compared with systemic opioid analgesia but the optimal technique to provide best analgesia with minimal adverse effects remains unclear. They carried out an observer-blinded randomized trial of side-directed epidural infusion with lumbar plexus infusion after total knee arthroplasty.

The results of the present study agree with the results of _Williams et al (2007)_ that continuous perineural femoral analgesia has been reported to reduce numeric rating pain scores (NRS, scale 0-10) after anterior cruciate ligament reconstruction (ACLR). In their study, they determined rebound pain scores in autograft ACLR outpatients after nerve block analgesia resolved. After standardized spinal anesthesia and perioperative multimodal analgesia, patients received a femoral perineural catheter and 50 hours of saline or levobupivacaine. All patients received levobupivacaine (30 mL of 0.25% as a bolus) before the infusion.

_Harsha et al (2012)_ agree with us that regional analgesia is widely used for total knee replacement surgeries (TKR) as it has lesser side-effects and better analgesic efficacy when compared with traditional oral analgesics. Peripheral nerve blockade has also been utilized, including continuous infusion techniques. With the use of ultrasound, the needle and catheter placement can be done accurately under real-time guidance. This may prove a more suitable approach compared with the epidural technique. Post-operative analgesia in TKR patients was compared
between continuous epidural analgesia (CEA) and continuous femoral block (CFB) techniques. VAS scores and use of rescue analgesic were used as parameters. Secondary aims included comparison of rehabilitation scores and side-effects in the form hypotension, vomiting, itching and urinary retention. Forty-two patients fulfilling the study criteria were randomised into the CEA and CFB groups. In total, four patients: three in the CFB group and one in the CEA group, were excluded because of catheter migration. Mean VAS score at 6, 6–24, 24–48 and 48–72 h were considered. Significance was assessed at the 5% level. VAS scores were significantly high ($P=0.001$) in the femoral group at 6 h, after which there was a declining trend, and scores were essentially similar from 24 h. Common side-effects were more common in the CEA group. Our study shows that CFB gives equivalent analgesia compared with CEA in TKR patients with clinically meaningful decrease in side-effects.

**Barrington et al (2005)** disagree with us that “CFB provides equivalent analgesia compared to CEA after TKR, except for the initial 6 hours, during which time it was significantly inferior”, while in our study the two techniques was equivalent all through the study times. Their study also demonstrates that the common side-effects are more common with the epidural group compared with the femoral group. In one of the largest studies, they showed equivalent analgesia between the two techniques. The use of tramadol as a rescue analgesic mirrored the difference showed by VAS scores; however, this was not significant. Earlier studies using other opioids have shown similar results. The decreased efficacy of CFB compared with CEA in the first 6 h may be related to the sciatic nerve component for knee innervation, which was not blocked in the femoral group. Their observation showed that patients with CFB complained of pain in their calf. Anatomically, the knee joint
derives its nerve supply predominantly from the femoral nerve; however, there seems to be an important component from the sciatic nerve that manifests as pain related to calf and leg.

The meta analysis by **Fowler et al (2008)** indicated no difference in pain scores between CEA and peripheral nerve blocks (PNB), even when analyzed separately, with or without sciatic block, this finding agree with our study. In a study by **Ben-David et al (2004)**, 83% of the patients did not derive comparable analgesia with CFB alone and required addition of continuous sciatic infusion.

**Weber et al (2002)** reported that 67% of the patients who had a femoral block required sciatic block post-operatively. In fact, there are nearly an equal number of studies arguing sufficient and insufficient blockade with femoral blockade alone.

**Barrington et al (2005)** observed that the rehabilitation scores were similar in both groups at all times, as observed in other studies. However, the “unilateral blockade” achieved by CFB encourages early mobilization apart from passive and active mobilization of the operated limb. This was also observed by, The incidence of common side-effects observed with CEA was lower in the CFB group by more than half. Although a statistical difference could not be achieved, probably because of the number of subjects, it was clinically meaningful and perhaps the most evident difference, given the equivalent analgesia and rehabilitation achieved with both techniques. Patients having TKR are mostly beyond 50 years, and many suffer from cardiovascular disease requiring anticoagulant medications. CFB does not necessitate withholding of these medications as rigorously as needed for CEA, which means lesser risk of altering the physiological profile. Another deviation from the consensus opinion was the performance of PNB on anesthetized patients in our
study. Catheters are mostly inserted pre-operatively as a routine practice. Despite the theoretical concern of nerve injury, there are no prospective randomized controlled studies that compare the relative risks of PNB performed on anesthetized against conscious patients. In general, there is insufficient published data to lend support to either argument. In fact, an earlier audit done by the American Society for Regional Anesthesia had shown that the practice is common in adults and children.

In Philippe et al (2009) study, similar intensities of nerve stimulation were required in both the bupivacaine and the bupivacaine lidocaine groups.

In Capdevila et al (2002) The addition of obturator nerve block to femoral nerve block or a combined femoral and sciatic block has the potential to improve analgesia compared with femoral nerve block alone. The posterior approach to the lumbar plexus block should reach the femoral nerve, the obturator nerve and the lateral cutaneous nerve of thigh with a single injection.

In a recent magnetic resonance imaging (MRI) investigation of Mannion et al (2005) comparing the spread of local anesthetic solution with 2 different approaches to the posterior psoas compartment block, Mannion et al. showed that when using a nerve stimulator-guided technique aimed at eliciting contraction of the quadriceps muscle with cranial movement of the patella the contrast spreads within the psoas muscle along the fascial plane surrounding the femoral nerve and L2-L3 branches reaching the L2-L4 roots.

The results of the present study agree with the results of Marhofer et al (2000) as they traced the distribution of local anesthetic during a 3-in-1 block by means of MRI, and reported that the local anesthetic blocks the femoral nerve directly, while the lateral femoral cutaneous nerve may
be partially blocked through a lateral spread of the injected anesthetic, and the anterior branch of the obturator nerve by slightly medial spread.

Unless they used different drugs other than ours Soto Mesa et al (2011) performed a prospective randomised study of patients subjected to knee replacement with subarachnoid anaesthesia. The postoperative analgesia consisted of one of the following techniques: Femoral nerve block with a single dose of 30mL of 0.5% ropivacaine, or that dose plus a continuous infusion via a femoral catheter of 0.375% ropivacaine 6ml/h for 48h. The demographic, anaesthetic and surgical variables were recorded, along with the pain intensity using a visual analogue scale, opioid use, and complications at 24 and 48h after surgery.

Soto Mesa et al (20011) agreed with us that the pain intensity was lower in the group that had continuous femoral block, particularly at 48h, compared to the single-dose block, and with a lower use of rescue analgesia in the continuous femoral block. The incidence in secondary effects was similar, with a lower long-term sensory block being observed in the femoral block with a single dose.

The results of the present study agree with the results of White et al (2002) that patients receiving perineural local anesthetic achieved both clinically important and statistically significant reductions in resting and breakthrough pain scores while requiring fewer doses of oral analgesics. Patients who received perineural local anesthetic also experienced additional benefits related to improved analgesia. Zero to 30% of patients receiving perineural ropivacaine reported insomnia resulting from pain, compared with 60% to 70% of patients using only oral opioids. Related to this, patients receiving perineural ropivacaine awoke from sleep because of pain on average less than one time on the first postoperative night.
compared with 2.0 to 2.3 times for patients receiving perineural saline. Dramatically lower opioid consumption in patients receiving perineural local anesthetic resulted in fewer opioid-related side effects, including less frequent nausea, vomiting, pruritis, and sedation.

Singelyn et al (1998) agree with us that patients receiving perineural local anesthetic reported greater satisfaction with their postoperative analgesia (0 to 10) of 8.8 to 9.8 compared with 5.5 to 7.7 for patients receiving placebo. Similar benefits have been demonstrated in comparable studies of patients having painful orthopedic surgeries such as arthroplasties of the knee, hip, and shoulder. Two unmasked but randomized studies suggest that continuous femoral nerve blocks after total knee arthroplasty result in a more rapid resumption of knee flexion.

Petersen et al (1991) agree with us that a lumbar plexus infusion is a reasonable alternative to epidural anesthesia for total knee arthroplasty. The lower incidence of bladder catheterization may be seen as a significant benefit since many orthopedic surgeons are reluctant to catheterize in this group of patients because of concerns regarding joint infection.

As regards time of first request for analgesia in this study there was statistically significant difference between the control group (general group) and the other 4 groups p<0.001, as there was a great difference between the general group (much earlier request) of systemic analgesic (pethedine 50 mg) and both combined epidural and combined femoral groups (much delayed request) of LA bolus, also there was statistically significant difference(p<0.001) between groups without clonidine (earlier request) and groups with clonidine–bupivacaine (delayed...
request) and there was no significant difference between combined epidural & combined femoral groups.

As regards number of requests/24 hours for analgesia by local postoperative boluses in this study there was statistically significant difference (p<0.001) between groups without clonidine (increased number of requests) and groups with clonidine–bupivacaine (decreased number of requests) and there was no significant difference between combined epidural & combined femoral groups.

As regards total dose of local anesthetic /24 hours for both intraoperative anesthesia and postoperative analgesia in this study there was statistically significant difference (p<0.001) between groups without clonidine (increased dose) and groups with clonidine–bupivacaine (decreased dose) and there was no significant difference between combined epidural & combined femoral groups.

*Elia et al* (2008) agree with us that clonidine is a frequently used adjuvant to local anesthetics (LA). The analgesic properties of clonidine when administered intrathecally or epidurally have been demonstrated; they seem to be attributable to its α₂ agonist properties. The benefit of adding clonidine to LAs for peripheral nerve blocks is less clear, although it is widely believed that clonidine improves quality and duration of a LA block.

*Sakaguchi et al* (2000) agree with us that a variety of adjuvants may be added to epidural infusions to enhance analgesia while
minimizing side effects. Clonidine mediates its analgesic effects primarily through the spinal dorsal horn \(\alpha_2\)-receptors on primary afferents and interneurons, as well as the descending noradrenergic pathway, and the epidural dose typically used ranges from 5 to 20 µg/hr.

**Shivinder et al (2010)** study compared the effects of clonidine added to bupivacaine with bupivacaine alone on supraclavicular brachial plexus block and observed the side-effects of both the groups. Two groups of 25 patients each were investigated using (i) 40 ml of bupivacaine 0.25% plus 0.150 mg of clonidine and (ii) 40 ml of bupivacaine 0.25% plus 1 ml of NaCl 0.9, respectively. The onset of motor and sensory block and duration of sensory block were recorded along with monitoring of heart rate, non-invasive blood pressure, oxygen saturation and sedation. It was observed that addition of clonidine to bupivacaine resulted in faster onset of sensory block, they agree with us that addition of clonidine to bupivacaine resulted in longer duration of analgesia (as assessed by visual analogue score), prolongation of the motor block, they agree with us that addition of clonidine to bupivacaine resulted in prolongation of the duration of recovery of sensation and no association with any hemodynamic changes (heart rate and blood pressure), sedation or any other adverse effects. These findings suggest that clonidine added to bupivacaine is an attractive option for improving the quality and duration of supraclavicular brachial plexus block in upper limb surgeries.
SUMMERY

Regional anesthesia at the lower limb has been demonstrated to be a valuable technique for the management of immediate postoperative pain after orthopedic surgery. In addition, postoperative continuous femoral block has been shown to hasten recovery and rehabilitation processes and therefore decrease the length of hospital stay of knee surgery patients. Continuous lower extremity blocks provide superior analgesia with fewer side effects, improve perioperative outcomes, and accelerate hospital dismissal after major joint replacement.

Analgesia delivered through an indwelling epidural catheter is a safe and effective method for management of acute postoperative pain. Postoperative epidural analgesia can provide analgesia superior to that with systemic opioids. Intra operative use of the epidural catheter as part of a combined epidural-general anesthetic technique results in less pain and faster patient recovery immediately after surgery than general anesthesia followed by systemic opioids does. Each of these options may affect the quality of postoperative analgesia, patient-reported outcomes, and even rates of morbidity and mortality.

In this study we compared between epidural and continuous femoral block in knee surgery 100 patients of ASA physical status I-II scheduled for elective knee surgery in The University Hospital Benha Faculty of Medicine.

Patients were randomly allocated into 3 main groups Group I , Group II and Group III as following :

**Group I:** Received general anesthesia alone (20 patients).

**Group II:** Which received combined general epidural anesthesia, This group was further subdivided into 2 subgroups IIA and IIB:

**Subgroup IIA:** Epidural anesthesia was conducted using 10 ml of bupivacaine 0.25% (2.5 mg/ml solution) followed by continuous infusion
at a rate of 10 ml/hour till the end of operation then postoperative boluses on request.

**Subgroup IIB:** Clonidine was added to LA solution at a dose of 1 µg/mL epidural anesthesia was conducted using 10 ml of bupivacaine0.25% (2.5 mg/ml solution)+clonidine 1 µg/mL followed by continuous infusion at a rate of 10 ml/hour) till the end of operation then postoperative boluses on request.

**Group III:** Received continuous femoral block and was further subdivided into 2 subgroups IIIA and IIIB:

**Subgroup IIIA:** Femoral anesthesia was conducted using 20 ml of bupivacaine 0.25% (2.5 mg/ml solution) followed by continuous infusion at a rate of 10 ml/hour till the end of operation then postoperative boluses on request.

**Subgroup IIIB:** Clonidine was added to LA solution at a dose of 1µg/mL femoral anesthesia was conducted using 20 ml of bupivacaine0.25% (2.5 mg/ml solution)+clonidine 1 µg/mL followed by continuous infusion at a rate of 10 ml/hour) till the end of operation then postoperative boluses on request.

Concerning demographic data there was no significant difference between the five groups.

Concerning intra operative data, first of them MAC there was statistically significant difference between the control group (general group) and the other 4 groups p<0.001, as MAC was much lower in combined general epidural groups & combined general femoral groups than in general only group (control group). This means that epidural& femoral anesthesia provides much more decrease in consumption of general anesthetic with decrease of their side effects.

As regards BP &HR in this study there was statistically significant difference between the control group (general group) and the other 4
groups p<0.001, as BP & HR were much lower in combined general epidural groups & combined general femoral groups than in general only group (control group).

Concerning post operative data, first of them VAS there was statistically significant difference between the control group (general group) and the other 4 groups p<0.001, as there was a great difference between the general group (much higher pain scores) and both combined epidural and combined femoral groups (much lower pain scores), also there was statistically significant difference between groups with additive (clonidine) namely group IIB& IIIB (lower VAS) and groups without clonidine namely group IIA & IIIA (higher VAS) and there was no significant difference between epidural and femoral groups.

As regards time of first request for analgesia there was statistically significant difference between the control group (general group) and the other 4 groups p<0.001, as there was a great difference between the general group (much earlier request) of systemic analgesic (pethedine 50 mg) and both combined epidural and combined femoral groups (much delayed request) of LA bolus, also there was statistically significant difference(p<0.001) between groups without clonidine (earlier request) and groups with clonidine–bupivacaine (delayed request) and there was no significant difference between combined epidural &combined femoral groups.

While in number of requests/24 hours for analgesia by local postoperative boluses there was statistically significant difference (p<0.001) between groups without clonidine (increased number of requests) and groups with clonidine–bupivacaine (decreased number of requests) and there was no significant difference between combined epidural &combined femoral groups.
As regards total dose of local anesthetic /24 hours for both intraoperative anesthesia and postoperative analgesia in this study there was statistically significant difference (p<0.001) between groups without clonidine (increased dose) and groups with clonidine–bupivacaine (decreased dose) and there was no significant difference between combined epidural & combined femoral groups.
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الملخص العربي

إن تخدير العصب الفخذي يعد من انجح الطرق في معالجة الألم أثناء وبعد عمليات مفصل الركبة. وان التخدير المستمر لهذا العصب قد يرتقه هائه على ازالة الألم ويقلل عدد أيام وجود المريض بالمستشفى وليس له أضرار تذكر.

بينما التخدير عن طريق قسطره خارج الام الجافيه للنخاع الشوكي هو أيضا طريقه أمنه وفعاله في إزالة ذلك الألم واستخدامه مقرنون بالتخدير الكلي يؤدي الى سرعة افاقه المريض مع عدم شعوره بالألم.

في هذه الدراسة تمت مقارنة الطرقتين المذكورتين انفا في مائة مريض خاضعين لعمليات في مفصل الركبة وتم تقسيم المجموعات كالتالي:

مجموعه(I) تتكون من 20 مريضا يتم تخديرهم كلما فقط.

مجموعه(II) تتكون من 40 مريضا يتم تخديرهم بالحقن المستمر خارج الام الجافيه مع التخدير الكلي، وتقسم الى:

- مجموعه (IIA) مخدر موضعي فقط (20 مريضا)
- مجموعه (IIB) مخدر موضعي مضاف اليه عقار الكلونيدين (20 مريضا)

مجموعه(III) تتكون من 40 مريضا يتم تخديرهم بالحقن المستمر للعصب الفخذي مع التخدير الكلي وتقسم الى:

- مجموعه (IIIA) مخدر موضعي فقط (20 مريضا)
- مجموعه (IIIB) مخدر موضعي مضاف اليه عقار الكلونيدين (20 مريضا)

واستنتاجنا ما يلي:

يؤدي استخدام التخدير المستمر للعصب الفخذي الي نتائج مقارنة لما يؤدي اليه استخدام التخدير خارج الام الجافيه من تسكن الألم بعد عمليات الركبة وكلا الطرقتين تؤديان الي تسكن الألم بشكل هائل بالمقارنة بالحالات التي يستخدم فيها تخدير كلي فقط.
ان اضافة عقار الكلونيدين الى المخدر الموضعي في كلا الطرقتين المذكورتين يؤدي الى زيادة مدة التسکین وقلل الألم كما يقلل عدد مرات حقن المخدر الموضعي وجرعته في اربع وعشرين ساعه. التخدير المستمر للعصب الفخذی يعد بديلا جيدا للتخدير خارج الأم الجافيه وله اثار جانبیه أقل كما يعطي استقرارا أكبر لضغط الدم وضربات القلب وماينتج عنه من مضاعفات أقل بكثير.
دراسة مقارنة بين التخدير الموضعى المستمر للعصب النخذي وخارج الأم الجافية لتسكين الألم في عمليات مفصل الركبة

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