“ULTRASOUND GUIDED FEMORO SCIATIC NEEVE BLOCK FOR LOWER LIMB SURGERIES: COMPARISON BETWEEN CLONIDINE AND DEXMEDETOMIDINE WITH LEVOBUPIVACAINE.”

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ABSTRACT

Introduction: Peripheral nerve blocks are effective for postoperative pain management in lower limb surgeries. The addition of adjuvants to local anesthetics can enhance the quality and duration of analgesia. This study aimed to compare the efficacy and safety of clonidine versus dexmedetomidine as adjuvants to levobupivacaine in ultrasound-guided femoro-sciatic nerve blocks for lower limb surgeries.

Methods: In this prospective, randomized, double-blind study, 90 ASA I-II patients scheduled for lower limb surgeries were randomly allocated into two groups. Group A (n=45) received levobupivacaine with clonidine (1 μg/kg), and Group B (n=45) received levobupivacaine with dexmedetomidine (1 μg/kg) for ultrasound-guided femoro-sciatic nerve blocks. Postoperative pain was assessed using Visual Analog Scale (VAS) scores at 0, 2, 4, 8, 12, and 24 hours. Secondary outcomes included hemodynamic parameters (heart rate, blood pressure), motor blockade (Bromage score), and side effects (bradycardia, hypotension, nausea/vomiting).

Results: Demographic parameters were comparable between the groups. VAS scores were significantly lower in the dexmedetomidine group compared to the clonidine group at all time points ($p<0.001$). Bromage scores, indicating motor blockade, were significantly higher in the clonidine group at 2, 4, and 8 hours ($p<0.001$). The dexmedetomidine group had a significantly higher incidence of bradycardia (33.3% vs. 15.6%, $p=0.050$) and hypotension (26.7% vs. 4.4%, $p=0.004$). Systolic blood pressure was significantly lower in the dexmedetomidine group at 4 and 8 hours ($p=0.009$ and $p=0.026$, respectively). Mean arterial pressure showed significant differences at multiple time points with variable patterns.

Conclusion: Dexmedetomidine provides superior analgesia compared to clonidine when used as an adjuvant to levobupivacaine in femoro-sciatic nerve blocks but is

associated with a higher incidence of cardiovascular side effects. Clonidine results in more intense motor blockade with a more favorable cardiovascular profile. The choice between these adjuvants should be individualized based on patient characteristics and surgical requirements.
Keywords: Clonidine; Dexmedetomidine; Levobupivacaine; Femoro-sciatic nerve block; Lower limb surgery; Ultrasound-guided; Postoperative analgesia; Adjuvants

INTRODUCTION

Lower limb surgeries encompass a wide array of procedures ranging from minor soft tissue operations to complex orthopedic interventions including knee replacements, ankle surgeries, and foot reconstructions. Historically, these procedures were predominantly performed under general anesthesia or neuraxial techniques such as spinal or epidural anesthesia. However, the field of regional anesthesia has witnessed remarkable advancements in recent decades, particularly with the integration of ultrasound guidance, which has revolutionized the practice of peripheral nerve blocks. Among these, femoro-sciatic nerve blocks have emerged as a cornerstone technique for providing effective "anesthesia and postoperative analgesia in patients undergoing lower limb surgeries. The utilization of ultrasound guidance has significantly enhanced the precision, efficacy, and safety profile of these blocks, allowing for real-time visualization of anatomical structures, needle advancement, and local anesthetic distribution," thereby minimizing the risk of complications while maximizing block success rate.[1]

Peripheral nerve blocks not only provide targeted anesthesia but also offer several advantages over general anesthesia, including reduced systemic effects, improved hemodynamic stability, decreased postoperative nausea and vomiting, enhanced postoperative pain management, and expedited recovery with reduced hospital stay. Femoral and sciatic nerve blocks, when performed in combination, provide comprehensive anesthesia for the majority of the lower extremity, making them particularly suitable for a wide spectrum of lower limb surgeries.[2] The femoral nerve, originating from the lumbar plexus (L2-L4), innervates the anterior thigh and provides sensory branches to the medial aspect of the lower leg via the saphenous nerve. Complementarily, the sciatic nerve, the largest peripheral nerve in the human body, arises from the sacral plexus (L4-S3) and provides motor and sensory innervation to

most of the posterior aspect of the thigh, as well as the leg and foot, with the exception of the medial aspect of the lower leg. Together, these two nerve blocks can effectively anesthetize approximately 90% of the lower limb, providing an excellent alternative to neuraxial or general anesthesia.[3]

"The advent of ultrasound-guided techniques has markedly transformed the landscape of regional anesthesia. Unlike traditional approaches that relied heavily on anatomical landmarks and nerve stimulation, ultrasound guidance allows direct visualization of neurovascular structures, enabling more precise needle placement and local anesthetic delivery." This has translated into higher success rates, faster onset times, reduced volumes of local anesthetic required, and decreased incidence of vascular punctures or nerve injuries. A meta-analysis by Salinas et al. demonstrated that ultrasound-guided peripheral nerve blocks resulted in a 29% improvement in block success rates compared to nerve stimulation techniques alone.[4] Furthermore, real-time visualization allows anesthesiologists to navigate anatomical variations, which are not uncommon in the inguinal and popliteal regions, thereby enhancing the reliability and reproducibility of femoro-sciatic blocks across diverse patient populations.

The choice of local anesthetic is pivotal in determining the quality and duration of the nerve block. Levobupivacaine, the S-enantiomer of bupivacaine, has gained prominence due to its favorable safety profile, particularly with respect to cardiac and central nervous system toxicity when compared to its racemic counterpart. Levobupivacaine provides prolonged sensory blockade with a duration of action ranging from 9 to 24 hours, depending on the concentration used and the specific nerve blocked. However, despite its advantages, the duration of analgesia provided by levobupivacaine alone may not be sufficient for the extended postoperative pain

management required following many lower limb surgeries.[5] Consequently, various adjuvants have been investigated to prolong the duration of peripheral nerve blocks, enhance the quality of anesthesia, and potentially reduce the dose and concentration of local anesthetics, thereby mitigating the risk of systemic toxicity.

Alpha-2 adrenergic receptor agonists, including clonidine and dexmedetomidine, have emerged as promising adjuvants in regional anesthesia. These agents exert their effects through multiple mechanisms including central sympatholysis, direct inhibition of peripheral nerve action potentials, local vasoconstriction prolonging the duration of local anesthetics at the site of injection, and attenuation of inflammatory responses. Clonidine, one of the earliest alpha-2 agonists to be used as an adjuvant, has demonstrated efficacy in extending the duration of peripheral nerve blocks. “A systematic review by Pöpping et al. reported that the addition of clonidine to local anesthetics prolonged the duration of postoperative analgesia by approximately 2 hours, although this effect was associated with an increased incidence of hypotension and sedation.[6] The optimal dose of clonidine for peripheral nerve blocks remains a subject of debate,” with studies using doses ranging from 0.5 to 2 μg/kg, striking a balance between enhanced block characteristics and minimized systemic side effects.

More recently, dexmedetomidine, a highly selective alpha-2 adrenergic agonist with an alpha-2 selectivity ratio of 1620:1 (compared to 220:1 for clonidine), has garnered attention as a potential adjuvant for peripheral nerve blocks. Dexmedetomidine's higher selectivity for alpha-2 receptors potentially confers a more favorable side effect profile while preserving or even enhancing the analgesic efficacy. Experimental studies have demonstrated that dexmedetomidine, when used as an adjuvant to local anesthetics, not only prolongs the duration of sensory and motor blockade but also enhances the quality of analgesia through peripheral and central mechanisms.[7] The peripheral effects involve direct action on alpha-2A

adrenoceptors located on peripheral nerve endings, leading to hyperpolarization via potassium channel activation, which inhibits the firing of action potentials. Additionally, dexmedetomidine induces vasoconstriction through its action on alpha-2B receptors in the smooth muscle of blood vessels, potentially retarding the systemic absorption of local anesthetics and prolonging their local effect. Centrally, dexmedetomidine acts on alpha-2 receptors in the locus coeruleus and dorsal horn of the spinal cord, modulating pain transmission through descending noradrenergic inhibitory pathways.

Several clinical studies have investigated the efficacy of dexmedetomidine as an adjuvant in peripheral nerve blocks. A randomized controlled trial by Esmaoglu et al. demonstrated that the addition of 100 μg of dexmedetomidine to levobupivacaine for axillary brachial plexus block significantly prolonged the duration of both sensory and motor blockade without increasing the incidence of adverse effects.[8] Similarly, another study by Abdallah et al. found that dexmedetomidine, when added to bupivacaine for posterior tibial nerve block, extended the duration of analgesia by approximately 60% compared to bupivacaine alone.[9] However, the comparative efficacy and safety profile of clonidine versus dexmedetomidine as adjuvants to levobupivacaine specifically for femoro-sciatic nerve blocks in lower limb surgeries have not been comprehensively evaluated in the literature. While both agents share similar mechanisms of action, their differing pharmacological properties, particularly dexmedetomidine's higher alpha-2 selectivity, may translate into distinct clinical profiles in terms of efficacy, duration of action, and adverse effect incidence.

The clinical significance of prolonged postoperative analgesia following lower limb surgeries cannot be overstated. Effective pain management facilitates early mobilization, reduces the risk of venous thromboembolism, enhances patient satisfaction, and potentially decreases the length of hospital stay. Furthermore, adequate pain control is integral to preventing the transition from acute to chronic

pain, a not uncommon sequela following orthopedic surgeries. A study by Kehlet et al. reported that persistent pain following total knee arthroplasty could affect up to 15-20% of patients, underscoring the importance of optimal perioperative pain management strategies.[10] Prolonged regional anesthesia techniques, achieved through the judicious use of adjuvants, offer a promising approach to address these concerns while potentially reducing the reliance on systemic opioid analgesics, which are associated with a spectrum of adverse effects including respiratory depression, nausea, vomiting, constipation, and the risk of dependence.

The present study aims to comprehensively evaluate and compare the efficacy and safety profiles of clonidine and dexmedetomidine as adjuvants to levobupivacaine for ultrasound-guided femoro-sciatic nerve blocks in patients undergoing lower limb surgeries. By delineating the comparative advantages and potential drawbacks of these two alpha-2 agonists, this investigation seeks to provide evidence-based guidance for anesthesiologists in optimizing peripheral nerve block protocols. The primary endpoints will include the duration of sensory and motor blockade, quality of intraoperative anesthesia, postoperative pain scores, time to first analgesic request, total analgesic consumption over the “first 24 postoperative hours”, and incidence of adverse effects including hypotension, bradycardia, sedation, and respiratory depression. Secondary endpoints will encompass patient satisfaction, ease of block performance, time to hospital discharge, and functional recovery parameters. Through this systematic comparison, the study aspires to contribute to the evolving field of regional anesthesia, potentially refining practices to enhance patient outcomes following lower limb surgeries.

AIM & OBJECTIVES

Objective:

To evaluate the efficacy of FSN Block formulation Levobupivacaine 20ml + Clonidine (0.5 µg/kg) and Levobupivacaine 20 ml+ Dexmedetomidine (0.5 µg/kg), as the post operative analgesia up to 24 hrs after the surgery.

REVIEW OF LITERATURE

HISTORICAL BACKGROUND OF LOWER LIMB REGIONAL ANESTHESIA

Evolution of Femoral and Sciatic Nerve Blocks

The development of lower limb regional anesthesia techniques represents a significant advancement in the field of anesthesiology. The first documented femoral nerve block was performed by Crile in 1897, who used cocaine as the local anesthetic agent.[11] Sciatic nerve blockade emerged slightly later, with Labat publishing his classic technique in 1922, approaching the nerve in the gluteal region using surface landmarks.[12] These early techniques remained largely unchanged until the mid-20th century, relying on anatomical landmarks and paresthesia for nerve localization. The introduction of plastic cannulas in the 1960s facilitated continuous techniques, allowing prolonged postoperative analgesia. Winnie made substantial contributions to femoral nerve block technique in 1973 with his description of the "3-in-1 block," attempting to anesthetize " the femoral, obturator, and lateral femoral cutaneous nerves with a single injection.[13] This period marked the beginning of a more comprehensive approach to lower limb anesthesia, though the reliability of these techniques remained variable due to the limitations of landmark-based localization."

Landmark-based to Ultrasound-guided Techniques

The transition from landmark-based to precision-guided techniques represents perhaps the most significant advancement in regional anesthesia practice. Before the 1980s, nerve blocks relied solely on surface landmarks and elicitation of paresthesia, a technique associated with patient discomfort and variable success rates. The introduction of peripheral nerve stimulation in the 1980s improved precision by confirming needle proximity to target nerves through motor responses. However, the paradigm shift occurred with the adoption of ultrasound technology. Kapral et al. published one of the first studies on ultrasound-guided regional anesthesia in 1994, though initial applications focused on upper limb blocks.[14] By the early 2000s, ultrasound guidance was applied to lower limb blocks, with Marhofer et al. demonstrating improved efficacy compared to nerve stimulation techniques.[15] This technological transition dramatically improved block" success rates, reduced local anesthetic volumes, decreased performance time, and minimized complications. Ultrasound visualization allowed practitioners to observe neural structures, surrounding vasculature, and local anesthetic spread in real-time, transforming regional anesthesia from an essentially blind procedure to a visually-guided technique.

Development of Combined Femoro-sciatic Approach

The recognition that most lower limb surgeries require anesthesia of both the femoral and sciatic nerve distributions led to the development of combined femoro-sciatic approaches. While isolated blocks were initially performed separately, anesthesiologists began developing systematic approaches to provide comprehensive lower limb anesthesia more efficiently. Beck described a formal combined approach in the 1960s, though these early techniques still relied on landmark-based methods with variable success rates.[12] The development of continuous catheter techniques in the 1980s allowed for extended postoperative analgesia, particularly valuable for major orthopedic procedures such as total

knee arthroplasty. With the advent of ultrasound guidance, combined femoro-sciatic blocks became more accessible, with reduced performance time and improved success rates. Contemporary practice often employs a single-session, ultrasound-guided combined approach, using separate injections for each nerve complex but performed during the same procedural session. This approach provides comprehensive anesthesia for the entire lower limb while minimizing patient discomfort and procedural time. Modern combined femoro-sciatic techniques have become essential components of multimodal analgesia protocols and enhanced recovery pathways for lower limb surgeries.

LOWER LIMB NERVE INNERVATION

Anatomy and Physiology[16]

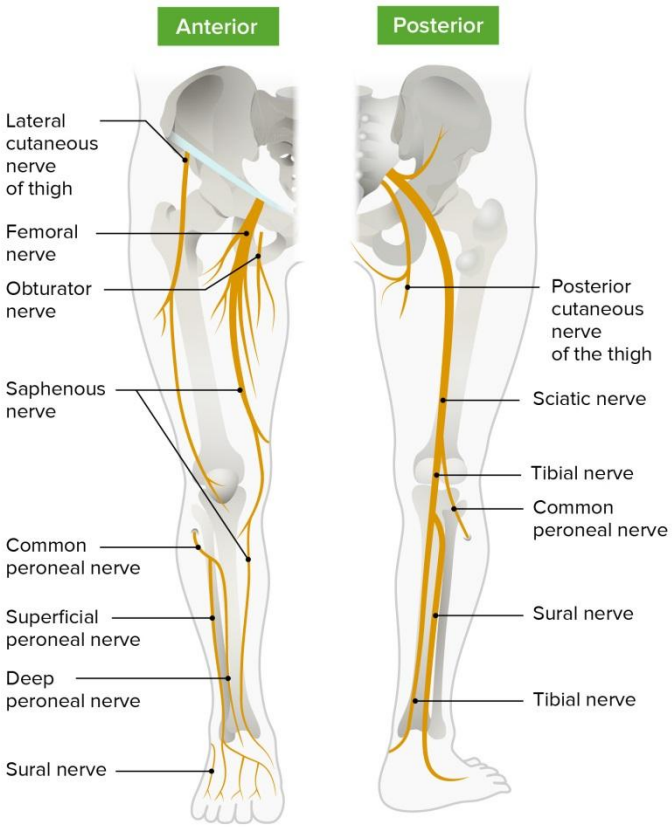
"The lumbosacral plexus divides into the femoral, lateral femoral cutaneous, obturator, and sciatic nerves that innervate the entire lower extremity. The femoral nerve provides sensation and motor function to the anterior thigh. The femoral nerve continues as the saphenous nerve, providing sensation to the ipsilateral medial leg and foot and a portion of the ipsilateral great toe. The LFCN supplies sensation to the lateral thigh. The sensory component of the obturator nerve supplies the medial thigh; the motor component supplies the thigh adductors.

Neither the lateral femoral cutaneous nor the obturator nerve have any sensory or motor input to the leg distal to the knee. The sciatic nerve runs with the posterior cutaneous nerve of the thigh and provides sensory and motor innervation to the posterior thigh. The sciatic nerve continues posteriorly and divides into the tibial and common peroneal nerves, just cephalad to the popliteal fossa, and provides sensory and motor innervation to the anterior, lateral, and posterior lower leg.

Five nerves provide sensory and motor to the foot. The saphenous nerve supplies sensation to the medial foot and a portion of the great toe. The deep peroneal nerve supplies

the web space between the great and second toes. The superficial peroneal nerve supplies most of the dorsum of the foot and toes, while the sural nerve supplies the lateral foot and a portion of the fifth toe. The posterior tibial nerve divides into the medial and lateral plantar nerves and supplies the sole and plantar surface of the toes."

Figure 1: Lower Limb Nerve Innervation



FEMORAL NERVE BLOCK

Anatomy and Physiology

One of the lumbar plexus's major branches is the femoral nerve. The femoral nerve enters the femoral triangle behind the inguinal ligament after emerging from the ventral rami of the L2, L3, and L4 spinal nerves. The femoral artery and femoral vein are located near the medial end of the triangle, which also includes the femoral nerve, which is the most lateral of the components.

The anterior and posterior divisions of the femoral nerve begin close to the circumflex artery. The sartorius muscle is innervated by the anterior division, which also produces the medial femoral cutaneous nerve. The quadriceps femoris muscle is innervated by the posterior division, which also produces the saphenous nerve.[16]

The femoral nerve supplies sensation to the anterior thigh and knee, as well as to the medial lower extremity beneath the knee, in addition to motor innervation. Sensation to the medial lower leg and foot is directly controlled by the saphenous nerve, a branch of the femoral nerve. At the level of the adductor canal and a few more distant locations, the saphenous nerve can be stopped independently. Stretching from the femoral triangle to the adductor magnus, the adductor canal is a musculoaponeurotic tube located in the mid-thigh. Proximal or high-volume adductor canal blocks may have an impact on the femoral nerve within the femoral region because of the anatomical relationship.[17]

Indications[17]

When doing surgery on the anterior side of the thigh, the femoral nerve block (FNB) is recommended. Additionally, it can be used in conjunction with an obturator block to offer complete lower extremity anaesthesia and with a sciatic nerve block to provide entire lower extremities coverage below the knee. After total knee replacement, pain reduction is achieved with both a single injection and ongoing infusions. In cases of patellar injuries, femur fractures, and femoral neck fractures, femoral nerve block is also helpful for analgesia. Femoral nerve blocks can be used either by themselves or in conjunction with other pain treatment techniques.

For individuals for whom general or neuraxial anaesthesia is contraindicated, lower extremity blocks can be helpful in giving focused anaesthesia to the hip, knee, ankle, or foot. Additionally, to enhance pain management and reduce the early postoperative opioid burden, lower extremity blocks are commonly used after surgery. Restoring mobility to patients who might otherwise be restricted by pain in the early postoperative phase is an additional advantage of lower extremity nerve blocks. This early mobilisation encourages early success in physical therapy and helps minimise problems like bedsores and venous thromboembolism.

Peripheral nerve blocks in the lower extremities can be used as a general anaesthetic or as a supplement to neuraxial or general anaesthesia. They have less side effects, like motor blockage, and offer efficient analgesia.

Ultrasound anatomy and nerve block technique

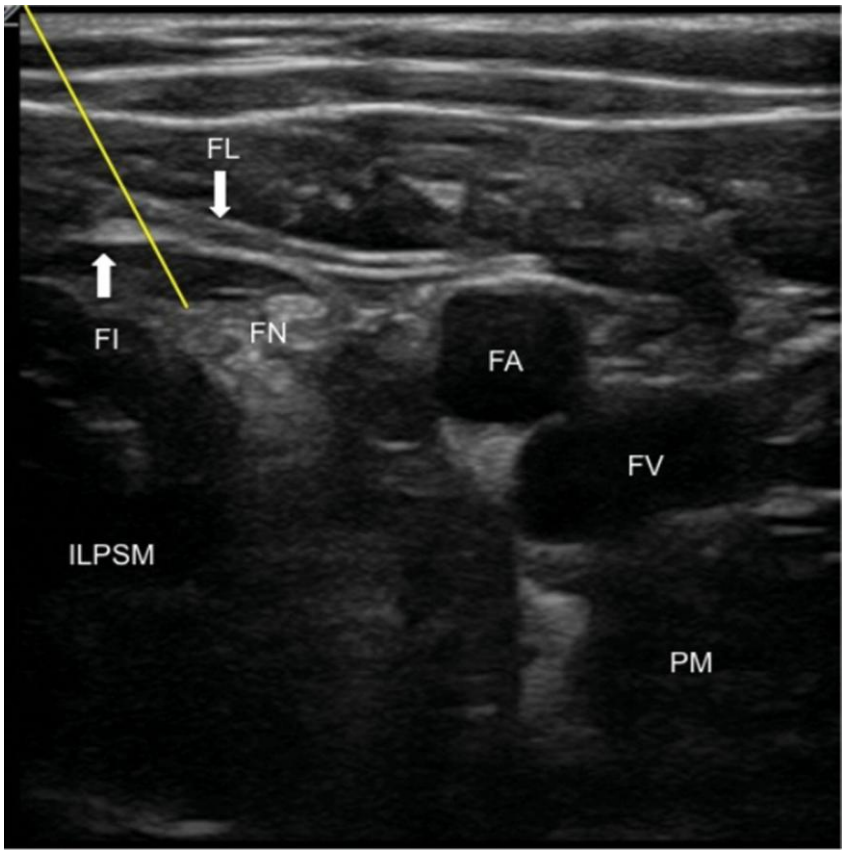
For blocks on both sides, the operator is on the right side of the patient while they are supine, and for a left-handed operator, the opposite is true. To ensure that the operator's line of sight, the needle, and the screen are all in a straight line, the ultrasound machine should be positioned on the other side.

It is necessary to install a linear high frequency (8–12 MHz) probe perpendicular to the femoral nerve's path and palpate the femoral artery behind the midpoint of the inguinal ligament and depth of picture set 3–5 cm. The transducer's medial to lateral sliding motions make it easier to see the pulsating femoral artery. The fascia iliaca, femoral artery, and the femoral nerve in a wedge-shaped area directly below and laterally are among the visible structures.

Usually hyperechoic, the femoral nerve is located in an inferior iliopsoas sulcus. The femoral nerve may exhibit anisotropic (directionally dependant) activity, and it may be easier to see the nerve if the probe is angled slightly cranially or caudally. The compressible femoral vein, which is situated infero-medially in relation to the pulsating femoral artery, and the distal divisions of the common femoral artery into superficial and profunda femoris arteries are among the additional structures seen. Even though the femoral nerve is located in a relatively superficial area, it can occasionally be challenging. Anatomical differences like the nerve's proximal division or comparable echogenicity to surrounding tissues could be the reason of this. In this case, using a peripheral nerve stimulator in conjunction with ultrasound may yield more details and validate the location of the nerve.

The inguinal area is exposed and cleaned for the block's conduct. A facet-tipped stimulating block needle is introduced either in-plane or out-of-plane to the ultrasonography probe after the femoral nerve has been located. Both methods penetrate the fascia lata and fascia iliaca, which is frequently felt as a double click. By using the PNS, quadriceps contractions and patellar movement in response to an electrical current of 0.2 to 0.5 mA suggest that the needle tip is close to the femoral nerve. A 1 ml hydrolocation test dosage can be used to verify needle insertion when the needle is seen next to the nerve. The needle should be moved since this could imply intraneural needle placement if the spread of LA cannot be seen and there is greater pressure on the syringe plunger. Despite the growing availability of modern instruments that provide objective pressure monitoring, a nurse assistant is frequently tasked with administering the injection rather than the operator. Spreading LA postero-laterally or antero-laterally is sufficient for the effectiveness of this block since the nerve fibres feeding the knee and patella are typically found on the lateral portion of the femoral nerve.[18]

Figure 2: "Ultrasound anatomy of in-plane femoral nerve block in the upper thigh. FL, fascia lata; FI, fascia iliaca; FN, femoral nerve; FA, femoral artery; FV, femoral vein; ILPSM, iliopsoas muscle; PM, pectineus muscle. The yellow line indicates needle path."



Complications

"There are always risks involved when performing a peripheral nerve bock. The following are complications that can result: nerve injury, allergic reaction, hematoma, infection, and local anesthetic systemic toxicity.[19] Also, patients should understand the risk of the nerve block not working successfully, and other forms of analgesia should be available. There is a small risk of temporary or permanent nerve injury, which can be caused by direct needle injury or intraneural injection. Given the possibility of complications, resuscitation equipment must be nearby in the event of local anesthetic systemic toxicity.[20]

A 20% lipid emulsion administration is effective for local anesthetic toxicity. A bolus dose of 1.5 mL/kg based on the lean body mass of lipid emulsion should be given over 1 minute and followed by an infusion of 0.25 mL/kg/min. This continuous infusion should continue until reaching hemodynamic stability. If hemodynamic stability is not obtained, then another bolus of 1.5 mL/kg (for a maximum of two total doses of 20% lipid emulsion), followed by a continuous infusion at the increased dose of 0.5 mL/kg/min should be considered. The 10% lipid emulsion in propofol should never be used as an alternative source for lipid emulsion therapy.[21]

Sciatic Nerve Block

The sciatic nerve is the workhorse of the lower extremity, supplying the vast majority of the motor and sensory function to the lower limb. It supplies motor function to the posterior thigh and all muscles below the knee. Sensory function is provided to the posterior thigh, posterior knee joint, and everything below the knee except a narrow band on the medial lower leg. This area is supplied by the saphenous nerve, which is derived from the lumbar plexus.[22]

Anatomy and Physiology

The sacral plexus originates from the L4-S3 nerve roots, and is located just lateral to the sacrum. It gives rise to five distal nerves: the sciatic nerve, posterior femoral nerve, superior gluteal nerve, inferior gluteal nerve, and pudendal nerve. The largest of these is the sciatic nerve, which courses beneath the gluteal muscles and then down the posterior leg.

Just above the popliteal crease, the sciatic nerve divides into the tibial and common peroneal nerves. These two nerves innervate almost the entire lower leg. While not completely accurate, it is useful to think of the tibial nerve as supplying the posterior lower leg and the plantar surface of the foot, while the common peroneal supplies the anterior lower leg and dorsal surface of the foot. The common peroneal nerve terminates as the deep and

superficial peroneal nerves of the foot. Likewise, the tibial nerve becomes the sural and posterior tibial nerves.

Regional anesthetic blockade of the sciatic nerve is possible at several anatomic locations. From proximal to distal, these sites are sacral plexus, classic transgluteal approach, subgluteal approach, anterior approach, and the popliteal approach. As with most other regional anesthetic techniques, ultrasound visualization has become the standard of practice.[23]

The sacral plexus approach is achieved by drawing a line between the posterior superior iliac spine (PSIS) and the ischial tuberosity on the side to be anesthetized, with the patient in the prone or lateral position. The sacral plexus is normally located approximately 8 cm distal to the PSIS along this line, although individual variation exists from 6 cm to 12 cm. While sacral plexus block is uncommonly used in regular clinical practice, ultrasound approaches have been well described. Of note is that the sacral plexus is the only peripheral sacral nerve location which is proximal enough to provide anesthesia for surgery of the hip when combined with lumbar plexus blockade. Sensory articular branches to the hip arise from the superior gluteal nerve, originating from the sacral plexus.

The transgluteal approach (aka Labat's technique) was the originally described and long preferred approach to sciatic nerve block because of its relatively consistent anatomic location. With the patient in Sim's position, the midpoint of a line from the greater trochanter of the hip to the posterior superior iliac spine is determined. A perpendicular to this first line is drawn from this midpoint. A second line is marked from the greater trochanter to the sacral hiatus. The spot where the perpendicular to the first line intersects the second line becomes the location of needle placement. While relatively consistent, the introduction of ultrasound into regional anesthetic practice has led to a shift away from the classic sciatic nerve block in favor of subgluteal, anterior, and popliteal approaches.

The subgluteal approach to sciatic nerve blockade has become the dominant approach to sciatic nerve block for procedures requiring complete knee or distal upper leg anesthesia (e.g., tourniquet placement). Visualizing along a line between the greater trochanter and ischial tuberosity utilizing ultrasound, the sciatic nerve is located in the subgluteal fascial plane above the quadratus femoris muscle. While this approach is usually performed in the lateral position, a supine variant with the hip flexed is also described.

The anterior sciatic approach occurs at the level of the lesser trochanter and has the advantage of being performed in the supine position. This is particularly useful when the patient cannot be positioned laterally. The thigh is externally rotated, and the knee flexed. Ultrasound visualization is used to locate the lesser trochanter of the femur. The sciatic nerve is then located both medial and deep to this bony landmark. Anesthetic results are similar to the subgluteal approach.

The popliteal approach is the most distal location for sciatic nerve blockade. The sciatic nerve is anesthetized just proximal to its division into the tibial nerve and the more lateral common peroneal nerve, approximately 6 cm above the popliteal crease. Originally described as a landmark-based blind technique, it has become a mainstay of knee and lower leg anesthesia and analgesia since the introduction of ultrasound visualization. The popliteal artery is located in the crease of the knee, as is the tibial nerve lying immediately posterior to it. The tibial nerve is continuously visualized as the probe is moved slowly in a proximal direction until the common peroneal nerve joins with it to form the sciatic nerve. A blockade utilizing the popliteal approach can be performed in the supine or lateral position. It is important to note that this approach will not relieve the pain from a tourniquet placed on the thigh due to the distal block location.

It is worth noting that selective tibial or common peroneal nerve blocks may be performed in the popliteal region. A selective tibial nerve block is one well-utilized technique

for relief of post total knee arthroplasty pain in the posterior knee or calf region. It also preserves the ability to dorsiflex the foot since the common peroneal nerve is spared. Dorsiflexion is crucial for postoperative ambulation, as it prevents falls from a dragging foot getting caught on the floor as it moves forward.

Any of the above approaches to the sciatic nerve will provide satisfactory anesthesia of the distal lower leg and foot (with the exception of the small strip of saphenous nerve sensory innervation previously mentioned). Several factors determine the choice of approach. The site of the surgical procedure, presence and location of a tourniquet, accessibility of block location, and acceptability of postoperative motor weakness are among the most important to consider.[24]

Complications

Potential complications related to sciatic nerve blocks include infection at the injection site, bleeding, nerve injury, and local anesthetic toxicity. Fortunately, all of these are rare, but simple precautions can minimize these occurrences if followed regularly. All nerve blocks should be performed under sterile technique to minimize the chance of infection at the injection site. Direct ultrasound visualization of the needle, nerve, and any nearby vascular structures minimizes the chance of nerve injury, local anesthetic toxicity, and accidental puncture of a blood vessel. Frequent negative aspiration during injection of local anesthetic, even when ultrasound visualization is utilized, is recommended.[25]

Ultrasound anatomy[18]

For scanning, the patient lies with the side to be blocked uppermost, flexed partially at the hip and knee. Using a curvi-linear low-frequency 3–9 MHz probe, a scan of the popliteal fossa is conducted first to identify the separate tibial and popliteal nerves lying superficial and posterior to the popliteal artery. Moving the probe proximally brings the two nerves together to form the sciatic nerve at a variable point above the popliteal crease. More

proximally, out with the popliteal fossa, the sciatic nerve is often difficult to visualize but is seen in the mid-thigh region as an oval structure with distinct fascicles with a fine line separating each nerve. It lies in the crease between biceps femoris laterally and semi-tendinosus and semi-membranosus medially. Towards the subgluteal region, the sciatic nerve characteristically changes shape from circular to triangular or flat. The sciatic nerve is approximately 4 cm deep in the subgluteal region.

Figure 3: Ultrasound anatomy of sciatic nerve in popliteal fossa. POST, posterior; ANT, anterior; MED, medial; LAT, lateral; TIB N, tibial nerve; C FIB N, common fibular nerve; PA, popliteal artery; PV, popliteal vein; ST/SM, semimembranosus/semitendinosus; BF, biceps femoris."

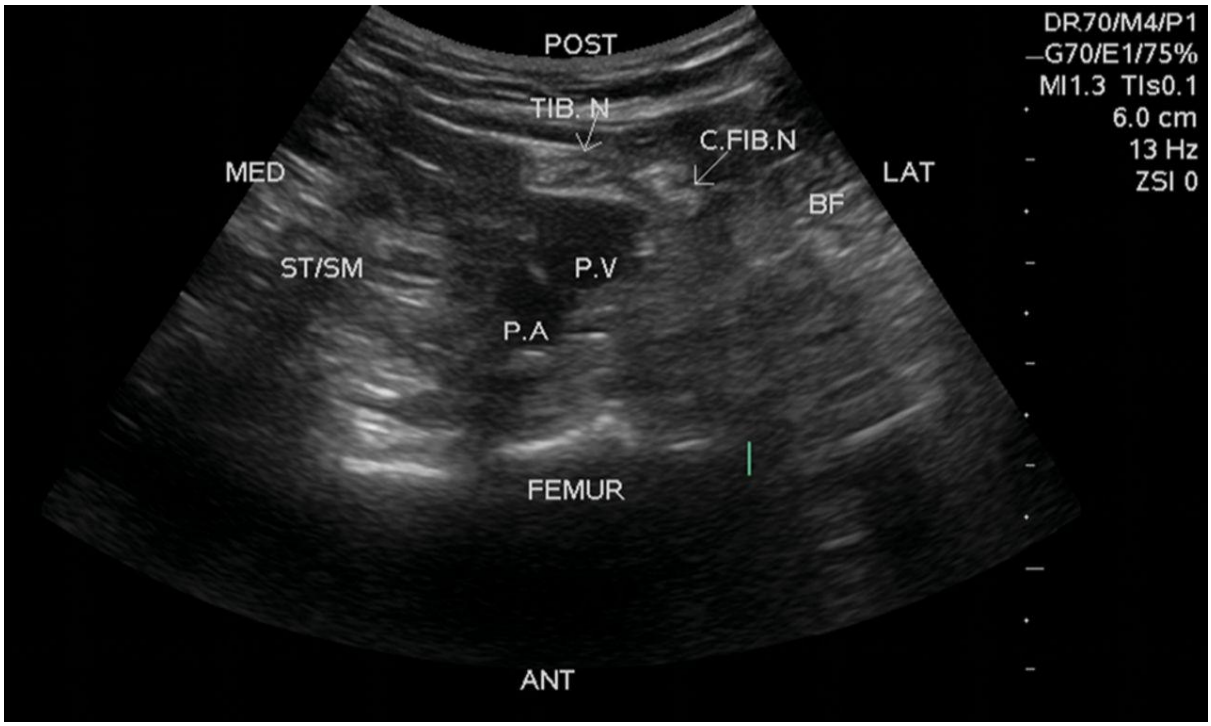


Figure 4: "Ultrasound anatomy of sciatic nerve (SCIATIC N) in lower-mid thigh level.

SM/ST, semimembranosus/semitendinosus; BF, biceps femoris."

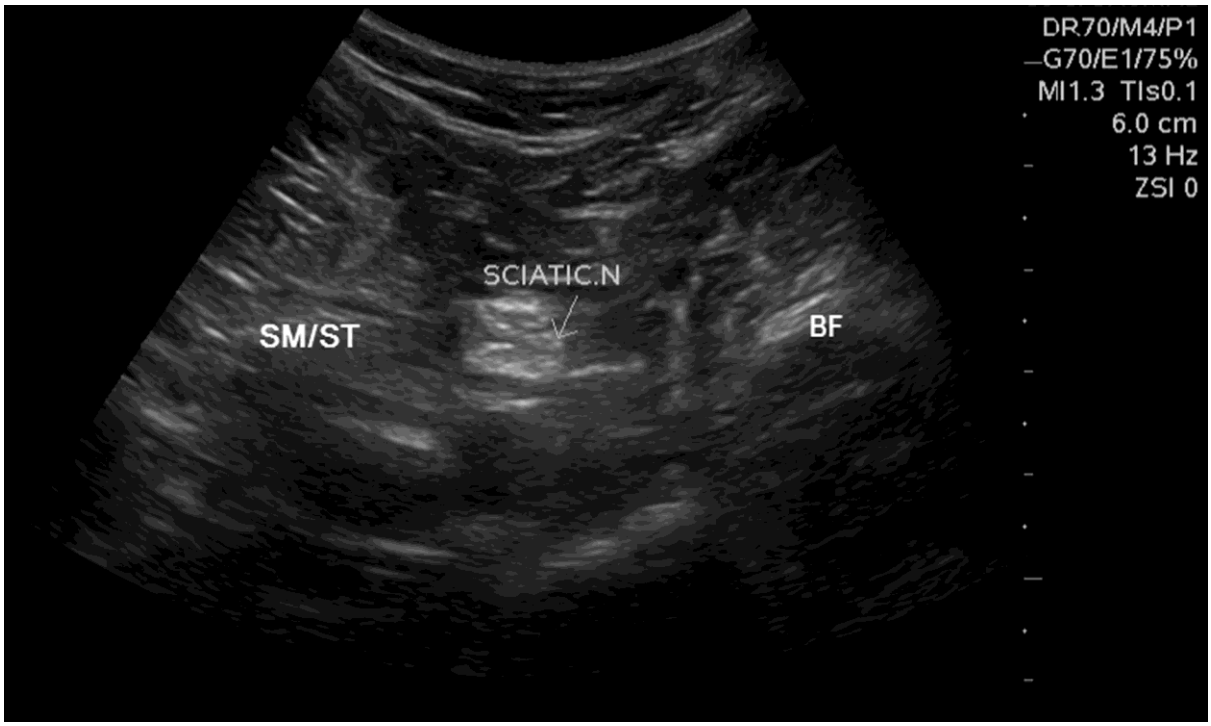
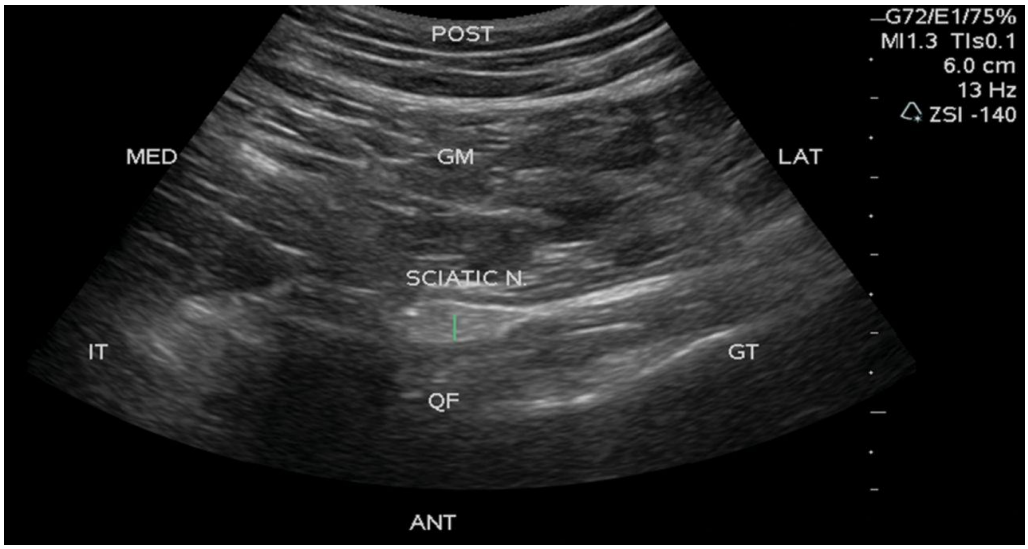


Figure 5: "Ultrasound anatomy of sciatic nerve (SCIATIC N) block (subgluteal approach). POST, posterior; ANT, anterior; MED, medial; LAT, lateral; GM, gluteus maximus; ST, semitendinosus; QF, quadratus femoris; GT, greater trochanter; IT, ischial tuberosity."



ULTRASOUND GUIDED REGIONAL ANESTHESIA

"Ultrasonography (US) as a means to guide peripheral nerve block (PNB) was first explored by anesthesiologists at the University of Vienna in the mid-1990s. Although radiologists had made use of ultrasound technology to guide needles for biopsy, the application of this imaging modality for PNB was novel at that time. The utility of ultrasound to facilitate a range regional anesthesia techniques including brachial plexus and femoral blocks was demonstrated. A decade later, colleagues from the University of Toronto, Canada, began to embrace this technology, further demonstrating its utility and describing in detail the sonoanatomy of the brachial plexus. Ultrasound guidance has become popular as a nerve localization tool in people, and its use during regional anesthesia has recently been called the "new gold standard."

Ultrasound is generated when multiple piezoelectric crystals inside a transducer (the probe) rapidly vibrate in response to an alternating electric current. This generates a mechanical form of energy that is simply a "high" frequency sound wave. Ultrasound then travels into the body where upon contact with various tissues, it can be reflected, refracted, and scattered. Structures that reflect ultrasound to a greater degree appear whiter, or more hyperechoic. Structures that reflect ultrasound to a lesser degree are described as hypoechoic and appear darker. Therefore, all structures appear as different shades of gray, allowing for specific tissue diagnosis (eg, needle from nerve).

Advantages of Ultrasound

The previously used surface anatomy-based techniques, such as nerve stimulation, palpation of landmarks, fascial "clicks," paresthesias, and transarterial approaches, did not allow for the monitoring of the disposition of the local anesthetic injectate. Ultrasound guidance, however, offers a number of important practical advantages for nerve block. Ultrasound allows visualization of the anatomy of the region of interest. This allows more

informed guidance for the needle pathway to the target while avoiding structures that might be damaged by the needle. Ultrasound also allows visualization of the needle tip as it is passed through the tissues, confirming alignment with the intended path, again reducing the likelihood of inadvertent needle trauma to unintended structures. Perhaps most important, real-time ultrasound imaging permits continual visualization of local anesthetic solution delivery to ensure proper distribution, with the potential for adjustment of the needle tip position as necessary to optimize local anesthetic distribution.

Introduction of ultrasound guidance in regional anesthesia has led to refinement of many nerve block techniques, expanded use of PNB, and greater acceptance by surgical colleagues and patients. The advantage of ultrasound guidance is that variation in individual patient anatomy no longer negatively affects block success rates. Compared with the use of nerve stimulation alone, ultrasound guidance has been shown to result in a higher rate of successful peripheral nerve blockade, decreased block set-up times and longer block durations.[25]

Nerve Imaging with Ultrasound

Because peripheral nerves can be difficult to identify from adjacent background structures, it is important to know all of their distinguishing features. The smallest peripheral nerves that have been imaged with ultrasound are the digital nerves.[26]These nerves are 2 mm in diameter and have been examined for the purpose of assessing nerve repair. While the limits of resolution continue to improve, most of the nerves for regional blockade can be imaged with ultrasound technology today. Nerves can have a round, oval, or triangular shape. Interestingly, a single nerve can have all three shapes along its nerve path as it travels between adjacent structures.[27]

Nerve identity can be confirmed by scanning along the known course of the nerve. Ultrasound can easily follow the oblique course of nerves, and this is difficult to accomplish with other imaging modalities such as magnetic resonance imaging. Short axis (transverse) scanning is preferred to follow a nerve along its course.

Advances in ultrasound technology will allow imaging of smaller and deeper nerves. Today, high-frequency broadband linear probes provide the best nerve imaging. Display of nerve sonograms is commonly performed with grayscale postprocessing maps, although there is recent evidence that color encoding received echoes improves musculoskeletal imaging.[28]

Needle Visibility

The primary factors that determine the ultrasound visibility of the needle are the insertion angle and gauge. At steep angles, backscatter from the needle rather than specular reflections is received by the ultrasound transducer. This results in marked reductions in needle tip visibility. Many authors have emphasized the critical importance of establishing needle tip visibility before advancing the needle when the in plane approach is used (see section entitled The In-plane Needle Approach). However, needle tip visibility is inherently

reduced at steep angles and may present problems. Entering the skin with the needle close to the transducer disturbs the surface contact and forces steep angles to the target.[29]

Large-bore needles are easier to visualize for two reasons. First, the larger cross-sectional area makes the needle easier to locate. Second, larger needles are less flexible and therefore less likely to bend out of the plane of imaging. One strategy has been to use large-bore (17-gauge) needles to promote needle tip visibility for deeper blocks.[30]

The role of acoustic background is substantial: The needle tip is best visualized within dark (anechoic) vessels or local anesthetic. A dark background, which can be created by low receiver gain, can improve needle tip visibility. Commercial modifications (coating or dimpling) to improve echogenicity of regional block needles are technically possible but have not been specifically marketed at this time.

Vascular punctures have been reported despite use of the in plane technique, emphasizing the importance of needle tip visibility in clinical practice. These inadvertent vascular punctures have occurred despite the fact that vessels are the easiest anatomical structures to identify with ultrasound. However, the vascular puncture rates with ultrasound guidance are probably lower than with other approaches to regional block.[31]

Local Anesthetic Solutions and Injection

Injection of quiescent (unagitated) solution can serve as reverse contrast, outlining the borders of the anesthetized nerve. Nerves will often be easier to identify after injection of undisturbed local anesthetic and sometimes can be seen to float freely within the injected solution. Injection of small amounts of air (0.3–0.5 ml) into the tissue through a needle can be used to identify the location of the tip.[32] Although bubbles are easy to identify sonographically and can serve as a useful marker of the needle tip, bubbles also can disperse in tissue and cause acoustic shadowing distally, becoming problematic. Therefore, all air bubbles are removed from the local anesthetic solution before injection. Most practitioners

elect not to use bicarbonate containing solutions of local anesthetic because these solutions evolve carbon dioxide, which obscures imaging.

One of the most important advantages of ultrasound imaging is the ability to reposition the needle after initial injection of local anesthetic. Test injections to visualize local anesthetic distribution should be small (1–2 ml). If the local anesthetic distribution is not seen on the monitoring screen immediately stop, aspirate, and move the transducer or needle (do not continue to inject because inadvertent intravascular injection is one of the possibilities). If the local anesthetic distribution does not adequately surround the nerves, the block needle can be repositioned, and the process of test injections can be continued. It is not necessary to contact nerves with the block needle to surround them with local anesthetic if the correct fascial planes are identified. After injection, the local anesthetic distribution can be assessed by sliding the transducer along the nerve path with the nerve viewed in short axis.

Imaging Planes and Approaches to Regional Block

Imaging Planes for Nerves

Nerves can be imaged in short axis or long axis. This nomenclature is familiar to many anesthesiologists because it is used in the field of transesophageal echocardiography. Similarly, the terms *transverse* and *longitudinal* have been used in the radiology literature. Ultrasound-guided blocks are generally performed with short axis imaging of nerves for several reasons. First, identification of peripheral nerves is relatively easy. Second, there is good resolution of the fascial barriers that surround nerves. Third, dynamic assessment and verification of circumferential distribution of local anesthetic with injection is possible. Finally, if the transducer moves slightly, the image is still workable (an oblique view of the nerve). For these reasons, short axis views of peripheral nerves for regional blocks have dominated practice at many institutions.

The Out-of-plane Needle Approach

The out-of-plane (OOP) technique involves inserting the needle so that it crosses the plane of imaging near the target. With this approach, the target is typically centered within the field of view and the depth noted. If the needle tip is not visualized, the endpoint for injection is not so clear and may require more dependence on small-volume test injections for visualization of adequate local anesthetic distribution. The OOP technique can be made similar to the in-plane (IP) technique (see section entitled The In-plane Needle Approach) with sliding and tilting of the transducerso as to follow the needle tip.

The In-plane Needle Approach

The needle can be inserted within the plane of imaging to visualize the entire shaft and tip (IP technique). For the IP approach, the imaged needle path should be maximized by placing the target on the side of the imaging field of view away from the approaching needle. The transducer can be manipulated as necessary to bring the needle into the plane of imaging. If the needle tip is not clearly identified within the plane of imaging, do not advance the needle. When the needle is in plane (longitudinal scan), the *in vivo* sonographic appearance will be hyperechoic, with parallel hyperechoic traces displayed away from the transducer. These hyperechoic traces result from reverberations inside the needle itself.[33]

Femoro-sciatic Nerve Block: Advantages and Disadvantages

Advantages

Femoro-sciatic nerve block provides comprehensive anesthesia for the entire lower limb through two targeted injections. This technique offers excellent surgical conditions with minimal physiological disturbance compared to neuraxial or general anesthesia. The block provides superior pain control with significantly reduced opioid requirements, decreasing opioid-related side effects such as nausea, vomiting, and respiratory depression. Patients

undergoing femoro-sciatic blocks generally experience less postoperative pain, leading to improved satisfaction scores and earlier hospital discharge. The technique preserves hemodynamic stability by avoiding sympathetic blockade that commonly occurs with neuraxial techniques, making it particularly valuable for elderly or cardiovascular-compromised patients. With ultrasound guidance, the success rates exceed 95% while minimizing the risk of complications like vascular puncture or nerve injury. For ambulatory procedures, femoro-sciatic blocks facilitate same-day discharge by providing extended postoperative analgesia without affecting consciousness or requiring intensive monitoring.[34,35]

Disadvantages

Despite its advantages, femoro-sciatic nerve block presents several limitations. The technique requires specialized equipment and advanced training, particularly for ultrasound-guided approaches, limiting its availability in some practice settings. Performing two separate blocks increases procedural time compared to single-injection techniques like spinal anesthesia. The resulting motor blockade can delay mobilization and physiotherapy, potentially conflicting with enhanced recovery protocols that emphasize early ambulation. Falls risk presents a significant concern, particularly in outpatient settings, as patients may attempt to bear weight on a functionally anesthetized limb. With a typical duration of 12-24 hours, the block's offset may coincide with peak pain periods, requiring careful planning of multimodal analgesia transitions. Block failure, though uncommon with ultrasound guidance, necessitates alternative analgesia plans. Rare but serious complications include local anesthetic systemic toxicity, nerve injury, and infection. Additionally, the technique is contraindicated in patients with local infection, coagulopathy, or significant anatomical distortion, and may be technically challenging in obese patients where ultrasound visualization is limited.[36,37]

Anesthetic Agents used

The two commonly used LA agents in the UK are ropivacaine and levobupivacaine. Both are chiral agents associated with less systemic toxicity than bupivacaine. Nevertheless, the efficacy and side-effects of both drugs are directly attributable to the blockade of sodium and potassium channels and therefore each individual treatment should take account of the maximal licensed dose, age, co-morbidity, location of block, and the use of epinephrine, albeit the latter is not routinely used for lower limb blocks.[18]

ADJUVANTS IN REGIONAL ANESTHESIA [38]

The pain transmission mechanism's complexity within both central and peripheral nervous systems necessitates a multimodal approach to analgesia. Adding adjuvant medications to local anesthetics for peripheral nerve blocks (PNBs) enhances and prolongs analgesia while reducing local anesthetic dose requirements, thereby minimizing potential toxicity. Various adjuvants including opioids, NSAIDs, and α2-agonists demonstrate synergistic effects with local anesthetics, without neurotoxicity at clinical doses, though they may produce side effects like hypotension, sedation, and bradycardia.

This multimodal approach is particularly valuable in outpatient and day surgery settings where prolonged analgesia is crucial and helps avoid continuous catheter placement, reducing infection risks. Despite their widespread clinical use, adjuvants remain off-label for PNBs without FDA approval, requiring anesthesiologists to carefully weigh benefits against risks. Evidence supports the use of buprenorphine, dexmedetomidine, and dexamethasone as adjuvants with favorable benefit-to-risk profiles, though debate within the medical community continues regarding their optimal application.”

Adjuvants Classification

“Adjuvants are classified according to their mode of action, application, and other parameters. The major categories of adjuvants are as follows”:

“Opioids

- *Buprenorphine*
- *Morphine*
- *Fentanyl*
- *Sufentanyl*
- *Tramadol*

Vasoactive agents/alpha-2 agonist

- *Clonidine*
- *Epinephrine*
- *Dexmedetomidine*

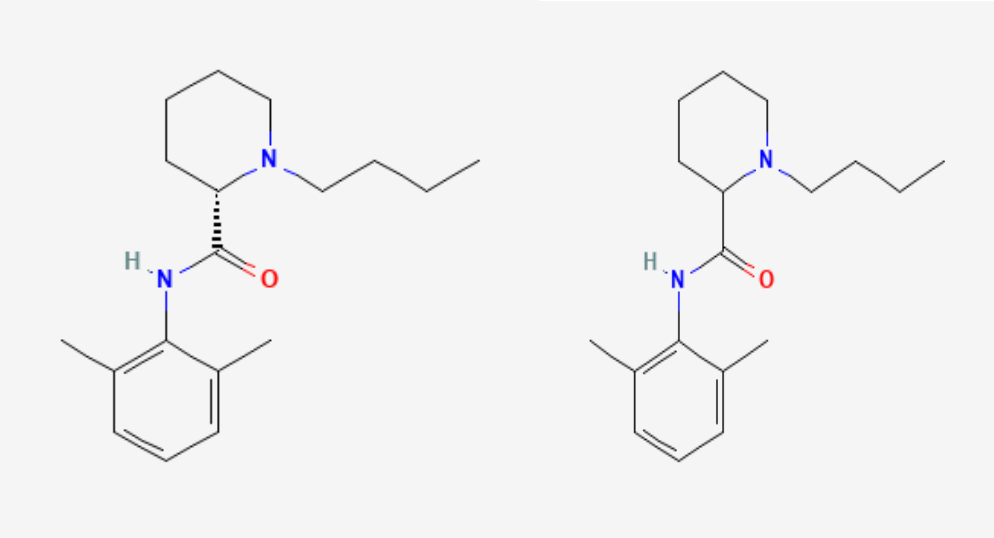
Anti-inflammatory agents/Steroids

- *Dexamethasone*
- Verapamil
- Ketorolac
- Methylprednisolone
- Adenosine

Other additives

- Ketamine
- Midazolam
- Neostigmine
- Magnesium
- Sodium bicarbonate”

PHARMACOLOGY OF BUPIVACAINE



Levobupivacaine and Bupivacaine

Indications

"Bupivacaine is a potent local anesthetic with unique characteristics from the amide group of local anesthetics, first discovered in 1957. Local anesthetics are used in regional anesthesia, epidural anesthesia, spinal anesthesia, and local infiltration. Local anesthetics generally block the generation of an action potential in nerve cells by increasing the threshold for electrical excitation. The progression of anesthesia is dependent on factors such as the diameter, degree of myelination, and conduction velocity of nerve fibers. In clinical practice, the order of a loss of nerve function is as follows:

1. Pain
2. Temperature
3. Touch
4. Proprioception
5. Skeletal muscle tone

Mechanism of Action

All local anesthetics contain three structural components: an aromatic ring, a connecting group which is either an ester (procaine) or an amide (bupivacaine), and an ionizable amine group. In addition, all LAs have two chemical properties that determine their activity:

1. Lipid solubility
2. Ionization constant (pKa)

Lipid solubility determines potency, duration of action, and plasma-protein binding of local anesthetics. Local anesthetics enter nerve fibers as a neutral-free base. Ionized forms and the cationic form blocks conduction by their interaction on the inner surface of the Na+ channel. Moreover, LAs with lower pKa has a more rapid onset of action, meaning more of it exists in an uncharged form, which renders faster diffusion to the cytoplasmic side of the Na+ channel.

Na+ channels are membrane proteins that propagate action potentials in axons, dendrites, and muscle tissue. They initiate and maintain membrane potential in specialized heart and brain cells. Depending on the tissue Na+, channels contain one larger alpha subunit and one or two smaller beta subunits.

The alpha subunit, the site of ion conduction, and local anesthetic binding have four similar domains, each with six alpha-helical membrane-spanning segments. The external surface of the alpha-subunit is heavily glycosylated, which allows the channel to orient properly within the cytoplasmic membrane. In contrast to local anesthetics, scorpion toxins and tetrodotoxin have binding sites on the extracellular surface of the Na+ channel.

Conduction of nerve impulses is through the generation of an action potential along an axon — local anesthesia results when LAs bind the Na+ channel and inhibit the Na+ permeability necessary for the action potential. Local anesthetics selectively inhibit the open form of voltage-gated Na+ channels. Na+ channel blockade results in the decrease or

elimination of conduction in vascular smooth muscle, leading to relaxation. In the heart, this leads to decreased pacemaker activity and prolongation of the refractory period. This action is unique to bupivacaine due to its decreased rate of dissociation from blocked sodium channels, which leads to prolongation of the maximal rate of depolarization (Vmax) and the potential for ventricular arrhythmias. Also, LAs produce a dose-dependent myocardial depression and interference with Ca2+ signaling within the cardiac muscle because they also bind and inhibit cardiac voltage-gated Ca2+ and K+ channels.

Local anesthetics also bind beta-adrenergic receptors and inhibit epinephrine-stimulated cAMP formation, which can explain the refractoriness of bupivacaine CV toxicity to standard resuscitation guidelines. In the central nervous system (CNS), local anesthetics may cause increased excitability, followed by its depression.

Neuronal tissues have different susceptibility to local anesthetics. Depolarizing currents in nerves move along nodes of Ranvier, and 2 to 3 nodes must be blocked to impair neuronal conduction completely. Smaller fibers have smaller internodal distances and, therefore, get blocked by local anesthetics more quickly.

Administration

Bupivacaine is offered in three different concentrations: 0.25%, 0.5%, and 0.75%.

Administration is by local infiltration (post-surgical analgesia), peripheral nerve blocks (dental or other minor surgical procedures, orthopedic surgery), spinal anesthesia (injected into the CSF to produce anesthesia for orthopedic surgery, abdominal surgery, or cesarean delivery), epidural anesthesia/analgesia for labor pain, and a caudal block (anesthesia and analgesia below the umbilicus, usually for pediatric surgery).

Adjuvants are often added to local anesthetics for nerve blocks to prolong the anesthetic effects compared to LA alone. Alpha 2 agonists such as clonidine or dexmedetomidine combined with the LA have been shown to increase the duration of

anesthesia significantly. Additionally, dexamethasone, when mixed with the local anesthetic for nerve blocks, has also been shown to increase the duration of anesthesia, although the mechanism is unclear as to whether it is a direct neural effect or simply the systemic effect of the steroid anti-inflammatory processes. With its N-methyl D-aspartate receptor antagonist effects, magnesium has also been associated with a prolonged duration of action of local anesthetics for nerve blocks. Studies are ongoing evaluating the effects of these and other potential adjuvants to LAs to prolong effectiveness while minimizing the risk of toxicity.

In the last decade, it has been shown that ultrasound-guided nerve blocks are associated with a decreased risk of local anesthetic toxicity. Presumably, visualization of the nerve and surrounding structures decreases the likelihood of injection into a vascular structure and increases the early recognition of this occurrence, thereby lessening the possibility of reaching toxic levels of bupivacaine in the bloodstream.

Adverse Effects

The dose of bupivacaine depends on the procedure, the vascularity of the tissue, the area, the number of segments blocked, the depth or duration of anesthesia needed, and the patient's physical condition. Bupivacaine may interact with ergot medications used for migraine headaches, blood thinners, antidepressants, or monoamine oxidase inhibitors. Immunologic reactions to local anesthetics are rare. Allergic reactions to preservative-free amide-type local anesthetics are rare and usually not reported. A true anaphylactic response appears more common with ester local anesthetics or preservatives; epinephrine-containing local anesthetics reactions are often misdiagnosed as allergic reactions. Patients may also react to preservatives such as methylparaben, which are included with local anesthetics.

Methemoglobinemia is typically associated with benzocaine or prilocaine; however, case reports exist implicating bupivacaine in rare instances. At low levels (1% to 3%), methemoglobinemia can be asymptomatic, but higher concentrations (10% to 40%) may

accompany cyanosis, cutaneous discoloration (gray), tachypnea, dyspnea, exercise intolerance, fatigue, dizziness, syncope, and weakness.

Some more common adverse effects include nausea, vomiting, chills or shivering, headache, back pain, dizziness, sexual dysfunction, restlessness, anxiety, vertigo, tinnitus, blurry vision, tremors which may precede more severe adverse effects such as convulsions, myoclonic jerks, coma, and cardiovascular collapse.

Contraindications

Contraindications include hypersensitivity to the drug or its components, hypersensitivity to amide anesthetics, infection at the injection site, obstetric paracervical block, obstetric anesthesia using 0.75% concentration, intravenous regional anesthesia, and intra-articular continuous infusion. Clinicians should exercise caution in patients with hypersensitivity to sulfites, liver impairment (the liver clears amides), kidney impairment, impaired cardiac function, heart block, hypovolemia, hypotension, and elderly, debilitated, or acutely ill patients.

LEVOBUPIVACAINE HOW IT DIFFERS FROM BUPIVACAINE

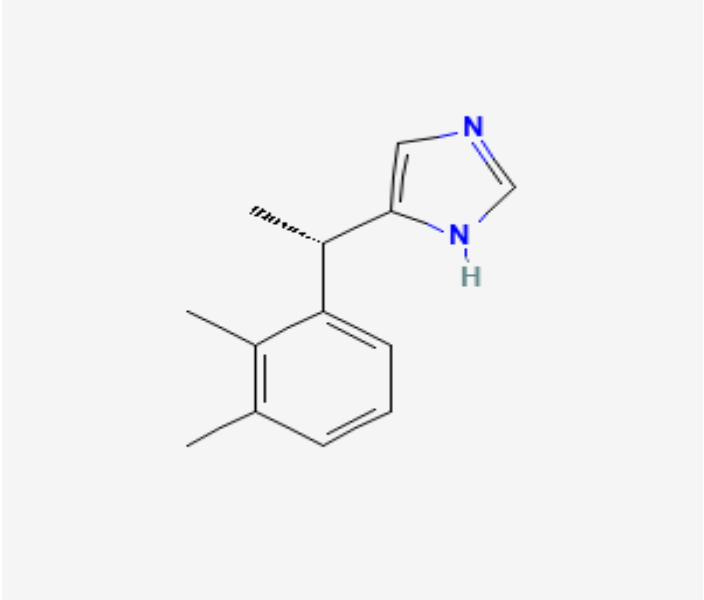
Levobupivacaine and bupivacaine are closely related local anesthetics, but they have some key differences:

1. Chemical structure:
    - Bupivacaine is a racemic mixture of two enantiomers (S and R forms)
    - Levobupivacaine is the pure S-enantiomer of bupivacaine
2. Toxicity:
    - Levobupivacaine has lower cardiac and central nervous system toxicity
    - This makes it safer, especially in higher doses or accidental intravascular injection
3. Potency:

- Levobupivacaine is slightly less potent than bupivacaine
- It may require slightly higher doses to achieve the same effect

4. Duration of action:
    - Levobupivacaine generally has a longer duration of action
5. Vasoconstrictive properties:
    - Levobupivacaine has greater intrinsic vasoconstrictive effects
    - This can prolong its action and reduce systemic absorption
6. Protein binding:
    - Levobupivacaine has higher protein binding, which contributes to its lower toxicity
7. Metabolism:
    - Levobupivacaine is metabolized more slowly, contributing to its longer duration
8. Regulatory status:
    - In some countries, bupivacaine may be more widely available or approved for more indications
9. Cost:
    - Levobupivacaine is often more expensive due to its purification process”

PHARMACOLOGY OF DEXMEDETOMIDINE[39,40]



“α2-adrenergic receptor (α2-AR) agonists have been successfully used in several clinical settings in view of diverse actions which include sedation, analgesia, anxiolysis, perioperative sympatholysis, cardiovascular stabilizing effects, reduced anesthetic requirements, and preservation of respiratory function. Dexmedetomidine is a relatively new drug approved at the end of 1999 by the Food and Drug Administration (FDA) for humans use for short-term sedation and analgesia (<24 hours) in the intensive care unit (ICU). Dexmedetomidine is a useful sedative agent with analgesic properties, hemodynamic stability and ability to recover respiratory function in mechanically ventilated patients facilitating early weaning. Besides being a new modality of sedation and analgesia in ICU patient management, it has been studied in several other perioperative settings.

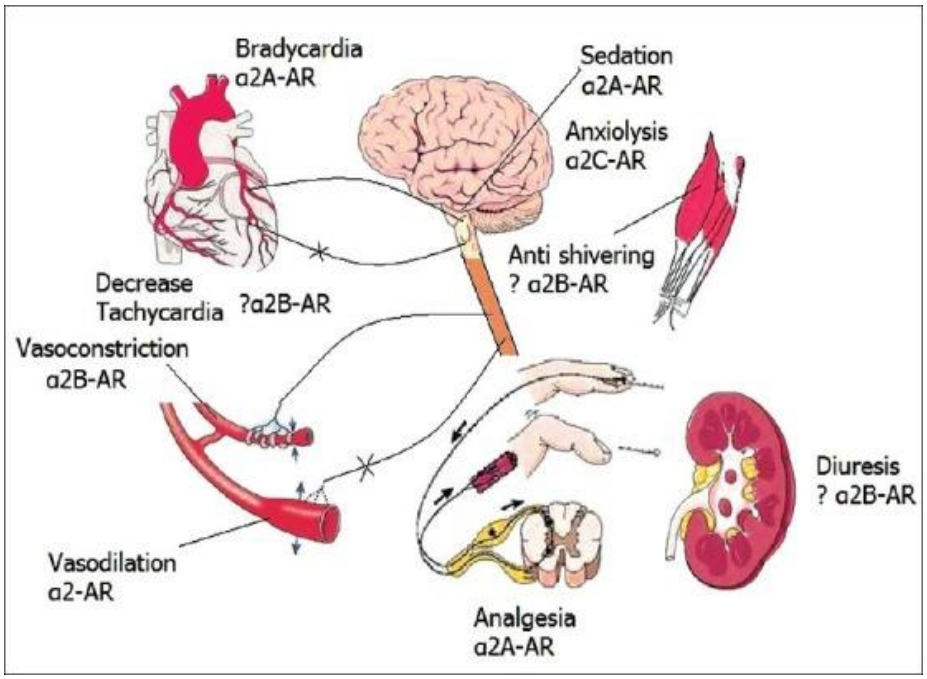
Chemical Structure

Dexmedetomidine is the dextrorotatory S-enantiomer of medetomidine, an agent used in veterinary medicine. It is chemically (S)-4-[1-(2,3-dimethylphenyl) ethyl]-3H-imidazole.

Mechanism Of Action

α2-AR agonists produce clinical effects after binding to G-Protein-coupled α2-AR, of which there are three subtypes (α2A, α2B, and α2C) with each having different physiological functions and pharmacological activities. These receptor subtypes are found ubiquitously in the central, peripheral, and autonomic nervous systems, as well as in vital organs and blood vessels. Dexmedetomidine is 8 to 10 times more selective towards α2-AR than clonidine. Neither clonidine nor dexmedetomidine is totally selective for any one of the α2-AR subtypes, but dexmedetomidine seems to have higher α2A-AR and α2C-AR affinity than clo Locus ceruleus of the brain stem is the principal site for the sedative action and spinal cord is the principal site for the analgesic action, both acting through α2A-AR. In the heart, the dominant action of α2-AR agonists is a decrease in tachycardia (through blocking cardioaccelerator nerve) and bradycardia via α2A-AR (through a vagomimetic action). In the peripheral vasculature, there is sympatholysis-mediated vasodilatation and smooth muscle cells receptor-mediated vasoconstriction. The mechanism for the antishivering and diuretic actions has yet to be established firmly".

Figure 2 Various α2-adrenergic receptorsnidine physiology.



Reduced bowel motility, decreased secretion, and decreased salivation in the gastrointestinal tract; contraction of vascular and other smooth muscle; inhibition of renin release, increased glomerular filtration; increased secretion of water and sodium in the kidney; decreased intraocular pressure; and decreased insulin release from the pancreas are all reactions to activation of the receptors in other regions. Dexmedetomidine circumvents some of the negative consequences of multiagent therapy by combining all of these effects.

Pharmacokinetics:

Absorption and Distribution

When given as an intravenous infusion for up to 24 hours, dexmedetomidine shows linear pharmacokinetics within the recommended dose range of 0.2 to 0.7 μg/kg/hr. With a distribution half-life of roughly six minutes and an elimination half-life of two hours, the dispersion phase is quick. The distribution's steady-state volume is 118 L. Protein binding averages 94%, is consistent across plasma concentrations, and is comparable in males and females. It exhibits very little protein binding displacement by medications like fentanyl, digoxin, theophylline, ketorolac, and lidocaine that are frequently used in anaesthesia and the intensive care unit. After a 10-minute infusion, the context-sensitive half-life is 4 minutes; after an 8-hour infusion, it is 250 minutes. A large amount of first-pass metabolism results in poor oral bioavailability. Nonetheless, dexmedetomidine given sublingually has a high bioavailability of 84%, suggesting a possible use in premedication and paediatric sedation.

Metabolism and Excretion

Direct N-glucuronidation and cytochrome P-450 (CYP 2A6)-mediated aliphatic hydroxylation result in nearly total biotransformation of dexmedetomidine into inactive metabolites. About 95% of metabolites are eliminated by urine, while 4% are eliminated through faeces. Due to their reduced rate of metabolism, patients with hepatic failure need to have their doses adjusted.

Clinical Pharmacology

Cardiovascular System

A brief hypertension phase and subsequent hypotension are the two phases of the blood pressure response elicited by dexmedetomidine. The two phases are thought to be mediated by two distinct α2-AR subtypes: the α2A-AR mediates hypotension, whereas the α-2B AR mediates the initial hypertensive phase. Anticholinergic medications (atropine, glycopyrrolate) have been shown to effectively treat bradycardia and sinus arrest in younger patients with elevated vagal tone.

Central nervous system

Although dexmedetomidine lowers cerebral blood flow and oxygen metabolism, its impact on intracranial pressure (ICP) is still unclear. In addition to its sedative, analgesic, and anxiolytic effects via the α2-AR, dexmedetomidine also improves cognitive function by modulating spatial working memory. According to studies, it may have a neuroprotective effect by lowering brain and circulating catecholamine levels, which would balance the ratio of cerebral oxygen supply, lower excitotoxicity, and improve perfusion in the ischaemic penumbra. It lowers the glutamate levels that cause cellular brain damage, particularly in subarachnoid haemorrhage. It has been demonstrated to reduce the morphologic and functional effects following traumatic and localised nervous system injuries.

Respiratory effects

The effects of dexmedetomidine on breathing seem to be comparable in magnitude to those observed during a state of heavy sleep. Even at high dosages, dexmedetomidine does not impair respiratory function. When administered to post-operative ICU patients who are breathing on their own, it has no negative effects on gas exchange or respiratory rate. It may make weaning and extubation easier for trauma/surgical intensive care unit patients who have failed prior weaning attempts due to agitation and hyperdynamic cardiopulmonary response

since it helps maintain sedation without cardiovascular instability or respiratory drive depression.

Endocrine and renal effects

Dexmedetomidine decreases catecholamine release and, consequently, the sympathetic response to surgery by activating peripheral presynaptic α2-AR.

Adverse Effects

Hypotension, hypertension, bradycardia, dry mouth, pyrexia, chills, pleural effusion, atelectasis, pulmonary oedema, hyperglycemia, hypocalcaemia, acidosis, and more are among the numerous adverse effects that have been documented. When dexmedetomidine is infused quickly (a loading dose of 1 μ/kg/hr if administered in less than 10 minutes), peripheral α2B-AR vasoconstriction may result in temporary hypertension. However, continued treatment mediated by central α2A-AR may result in bradycardia and hypotension due to a reduction in noradrenaline release from the sympathetic nervous system. A withdrawal syndrome characterised by anxiety, agitation, headaches, and hypertensive crisis may arise from abruptly stopping dexmedetomidine due to super sensitisation and upregulation of receptors caused by prolonged use. Patients with extensive cardiac block and ventricular dysfunction should not take dexmedetomidine. Because the FDA has categorised it as a category C pregnancy risk, pregnant women should use the medication extremely carefully.

Dexmedetomidine Clinical Applications

- **Pre-medication**

  Because of its sedative, anxiolytic, analgesic, sympatholytic, and stable haemodynamic profile, dexmedetomidine is utilised as an adjuvant for premedication, particularly in

patients who are prone to preoperative and perioperative stress. Dexmedetomidine can reduce oxygen use by up to 8% during the intraoperative phase and up to 17% during the postoperative phase. 15 minutes prior to surgery, a premedication dose of 0.33 to 0.67 mg/kg is administered intravenously (IV) to reduce the risk of bradycardia and hypotension.

- **Intra-operative use**

Through sympatholysis, dexmedetomidine reduces the haemodynamic stress response to intubation and extubation. Unlike other medications, it can be continued during the extubation interval because there is no respiratory depression. No matter how an anaesthetic is administered (intravenous, inhalation, or regional block), dexmedetomidine intensifies its anaesthetic effects. Lower amounts of dexmedetomidine used intraoperatively have decreased the need for further anaesthetics, the number of tachycardia treatment procedures, and the incidence of cardiac ischaemia. However, its use is limited by adverse effects such bradycardia and hypotension, which calls for pharmacological rescue therapy. Vasodilatation and myocardial depression, two characteristics of volatile anaesthetics, may be responsible for these effects. High doses of dexmedetomidine may impair myocardial function and blood pressure, or they may directly affect peripheral arteries, resulting in systemic and pulmonary hypertension.

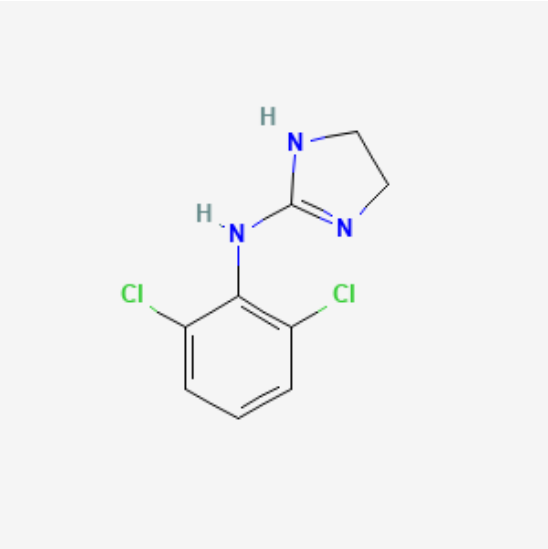
- **Locoregional analgesia**

Because dexmedetomidine is highly lipophilic, it can be quickly absorbed into the cerebrospinal fluid and bind to the spinal cord's α2-AR to produce analgesia. No matter how local anaesthetics are administered (e.g., epidural, caudal, or spinal), it extends the duration of both sensory and motor blockage. Although dexmedetomidine increases both central and peripheral neural blockade by local anaesthetics, its binding to α2A-AR is what causes the peripheral neural blockade. When it comes to dexmedetomidine,

effectively employed intraarticularly, brachial plexus block, and intravenous regional anaesthesia (IVRA).

- Sedation in intensive care unit
- Procedural sedation
- Controlled hypotension
- Analgesia
- Cardiac surgery
- Neurosurgery”

PHARMACOLOGY OF CLONIDINE



“Clonidine is an antihypertensive medication that acts on alpha-adrenergic and imidazoline receptor agonists. Clonidine is an antihypertensive drug that lowers blood pressure and heart rate by relaxing the arteries and increasing the blood supply to the heart; it has other FDA-approved indications such as treatment of attention deficit hyperactivity disorder (ADHD) in children (FDA approval

2010); management of tics commonly found with Tourette syndrome; and adjunct therapy for severing cancer-related pain.

Indications

Clonidine is a 40-year-old antihypertensive medication that acts as an agonist on alpha-adrenergic and imidazoline receptors. Clonidine is an antihypertensive drug that lowers blood pressure and heart rate by relaxing the arteries and increasing the blood supply to the heart; it has the following FDA-approved indications:

- Hypertension, as mentioned above; pediatric use for hypertension is off-label
- Treatment of attention deficit hyperactivity disorder (ADHD) in children (FDA approval 2010 for the extended-release dose form)
- Management of tics commonly found with Tourette syndrome
- Adjunct therapy for severing cancer-related pain
- As an adjunct in neonatal opioid withdrawal syndrome

Clonidine has multiple off-label uses, such as managing withdrawal symptoms from opioids, benzodiazepines, and alcohol and treating anxiety, insomnia, and post-traumatic stress disorder (PTSD).

Because of the effect of clonidine on the sympathetic nervous system, specifically, the reduction of circulating epinephrine, it has been used in many other aspects of medicine, for example, control of hot flashes in menopause, restless leg syndrome, and prophylaxis of vascular migraine headaches. Also, there is a test for phaeochromocytoma called the clonidine suppression test; in the lab, they measure the catecholamine levels before and after a dose of oral clonidine, which, in healthy people, should cause a decrease in the level of catecholamines in circulation.

Mechanism of Action

Clonidine hydrochloride is an imidazoline derivative that acts centrally on alpha-2 adrenergic as an agonist. The chemical name for clonidine is 2-((2,6-dichlorophenyl) amino)-2-imidazoline hydrochloride.

As an alpha-adrenergic agonist in the nucleus tractus solitarii (NTS), clonidine excites a pathway that inhibits excitatory cardiovascular neurons. Clonidine has an alpha-antagonist effect in the posterior hypothalamus and medulla. The final response is reduced sympathetic outflow from the central nervous system (CNS), which clinically causes a decrease in arterial blood pressure.

One of the theories about the mechanism of action of clonidine in the management of pain in the CNS is that many pain signals occur in the dorsal horn of the spinal cord and are sent to higher centers of the CNS. There is a release of norepinephrine from the descending inhibitory bulbospinal neurons that binds to alpha-2-receptors in the dorsal horn to decrease afferent pain transmission and produce analgesia. Therefore, drugs like clonidine that target alpha-2 receptors can influence the transmission of pain.

Epidural clonidine used as an adjunct to local anesthetics has three different mechanisms of action. First, the stimulation of alpha-2-receptors in the dorsal horn reduces pain transmission. Secondly, clonidine can cause local vasoconstriction that limits vascular removal of local epidural anesthetics. Lastly, clonidine enhances neuraxial opioids and, in combination with fentanyl, interacts in an additive manner, which can reduce the dose of each component by 60% for postoperative analgesia.

The exact mechanism of action of clonidine in the management of attention-deficit hyperactivity disorder (ADHD) is not clear, but it is possible prefrontal cortex brain activity is involved.

Clonidine has a half-life of between 6 and 20 hours (17 to 40 hours in cases of renal impairment.)

Injectable Solution

- Dosage: 100 mcg/ml, 500 mcg/ml
- Indications: epidural infusion form in cancer pain not controlled by opioid analgesics and as an adjunct in anesthesia
- The initial dose of 30 mcg/hr and titration is necessary for pain management or potential side effects.

Adverse Effects

Like any other medication, clonidine has the potential for short-term and long-term side effects. Some of the common side effects based on FDA reports include:

Common Reactions (tend to resolve with continued therapy)

- Abdominal pain
- Headache
- Hypotension
- Fatigue
- Nausea
- Emotional instability
- Constipation
- Xerostomia
- Diarrhea
- Sexual dysfunction
- Dizziness
- Sedation

Serious Reactions

- Angioedema
- Depression

- Hypersensitivity
- Atrioventricular (AV) block
- Bradycardia
- Syncope
- Severe hypotension

Note rebound hypertension and withdrawal symptoms if the medication is discontinued abruptly.

Other Symptoms

- Fever, headache
- Fatigue
- Bradycardia
- Congestive heart failure
- Decreased sexual activity
- Thrombocytopenia
- Agitation

Depression is one of the rarely reported side effects that can occur with the chronic use of clonidine; however, because of the variety of applications for this medication and also because of its slowly progressive onset, clinicians should monitor patients for signs of depression."

REVIEW OF RELATED ARTICLES

Charvin M et al (2020)[41] "To seek improved postoperative analgesia and care due to a long-acting combined femoral and sciatic nerve block in patients undergoing femoropopliteal bypass surgery. Patients were allocated to receive either an active nerve block with 20 ml of 0.375% levobupivacaine and clonidine 0.5 μg kg, or a simulated (sham) block only, but with local anaesthesia of the skin, before general anaesthesia. Patients in the active group received

less intra-operative sufentanil (median dose 25 vs. 41 μg), needed less morphine during the first 24 h (15 vs. 27 mg) and 72 (20 vs. 35 mg) postoperative hours, than in the control group. They also had less pain on movement, but pain at rest, the tissue oxygen saturation and other rehabilitation outcomes were unaffected by the treatment. Tolerance outcomes were also similar between groups. They concluded that **c**ombining the two regional blocks improves the quality of postoperative care in this frail population, probably by reducing the amount of peri-operative opioid.

Chaudhary SK et al (2016)[42] aimed to compare equal doses of clonidine or dexmedetomidine as an adjuvant to levobupivacaine in FSNB for post-operative analgesia. Duration of analgesia was prolonged with dexmedetomidine (10.17 ± 2.40 h) and clonidine (7.31 ± 1.76 h) as compared to control (4.16 ± 1.04 h, P = 0.00). Significantly lower pain scores were observed in dexmedetomidine group as compared to clonidine up to 8 h post-operatively. They concluded that **e**qual doses of clonidine or dexmedetomidine added to levobupivacaine prolonged the duration of analgesia, decreased requirement of rescue analgesia. Dexmedetomidine delays the requirement of rescue analgesics with better pain scores as compared to clonidine".

MATERIAL AND METHODS

- **Study design: "**Prospective, randomized, double-blind controlled trial
- **Study area:** Department of General Medicine, R.L. Jalappa Hospital and Research Centre, affiliated with Sri Devaraj Urs Medical College, Tamaka, Kolar.
- **Study period:** Research study was conducted from July 2023 to December 2024. Below is the work plan".

Table 1: Work plan of the study with percentage of allocation of study time and duration in months

Work plan	% of allocation of study time	Duration in months
Understanding the problem, preparation of questionnaire.	5-10%	July 2023 to September 2023
Pilot study, Validation of questionnaire, data collection and manipulation	Upto 80%	October 2023 to June 2024
Analysis and interpretation	5-10%	July 2024 to September 2024
Dissertation write-up and submission	5-10%	October 2024 to December 2024

- **Sample size**: “The sample size was calculated using Cohen's d-method with Family-Wise Error Rate (FWER). With a significance level (α) of 0.05 and power (1-β) of 0.80, the study was designed to detect a real effect between the groups. Since the study involved comparisons between two intervention groups, the FWER was adjusted to 0.025 (0.05/2). Using an effect size (d) of 0.6, which is slightly above the moderate effect size of 0.5, a sample size of 45 patients per group was determined to be adequate. This calculation was based on the method described by Suresh K.P. and Chandrasekhar S (2012) in their publication on sample size estimation and power analysis for clinical research studies in the Journal of Human Reproduction Science”.

- **Inclusion criteria:**

1. Age 20 to 60 years Males and Females.
2. ASA 1 and 2
3. Surgery of Foot and Leg.

- **Exclusion criteria:**

1. Refusal of the patient to block.
2. “History of heart, renal, or hepatic disease. Local infection at the area where the needle for block is to go in”.
3. Patients who have brady-arrythmia or are on beta blocker therapy.
4. Younger than 20 years old.
5. American Society of Anaesthesiologists physical status IV or V

Methodology

This prospective, randomized, double-blind controlled trial was conducted at “R.L. Jalappa Hospital and Research Centre, affiliated with Sri Devaraj Urs Medical College, Tamaka, Kolar. The study was conducted between May 2023 and October 2024 after

obtaining approval from the Institutional Ethics Committee. Written informed consent was obtained from all participants before enrollment in the study.

Randomization and Blinding

Participants who met the inclusion criteria were randomly allocated to one of two groups using systematic random sampling:

- Group A: Patients received ultrasound-guided femoro-sciatic nerve block with Levobupivacaine plus Clonidine (0.5 μg/kg).
- Group B: Patients received ultrasound-guided femoro-sciatic nerve block with Levobupivacaine plus Dexmedetomidine (0.5 μg/kg).

The randomization was performed using computer-generated random numbers. To ensure blinding, the anesthesiologist who prepared the study medications was not involved in either administering the block or assessing the outcomes. Similarly, the patients and the anesthesiologist who performed the block and evaluated the outcomes were blinded to the group allocation. The study medications were prepared in identical syringes labelled only with patient identification numbers.

Pre-Anesthetic Assessment

A detailed history was taken and complete physical examination was performed for all enrolled patients. Routine investigations including complete blood count, blood grouping, random blood sugar, blood urea, serum creatinine, serum electrolytes (sodium and potassium), and electrocardiogram were checked. Patients' demographic data including age, gender, height, weight, and ASA status were recorded.

Anesthetic Technique

On the day of surgery, all patients were transferred to the operating room where standard monitoring including electrocardiogram (ECG), non-invasive blood pressure (NIBP), and pulse oximetry (SpO2) was established. Baseline vital parameters including

heart rate, blood pressure, mean arterial pressure, and oxygen saturation were recorded. An intravenous line was secured with an 18G cannula, and intravenous fluids were administered as per the standard protocol.

All patients received subarachnoid block as the primary anesthetic technique for the lower limb surgery. After the completion of the surgical procedure and before the regression of spinal anesthesia, patients were administered the femoro-sciatic nerve block according to their group allocation.

Ultrasound-Guided Femoro-Sciatic Nerve Block Technique

The femoro-sciatic nerve block was performed under strict aseptic conditions using high-resolution ultrasound guidance. The procedure was performed by an experienced anesthesiologist with expertise in ultrasound-guided regional anesthesia.

Femoral Nerve Block

For the femoral nerve block, patients were positioned supine with the thigh slightly abducted. The femoral artery was palpated at the inguinal crease, and a high-frequency linear ultrasound transducer (8-13 MHz) was placed in a transverse orientation at this level. The femoral nerve was identified as a hyperechoic triangular structure lateral to the femoral artery, deep to the fascia iliaca. After skin infiltration with 1-2 ml of 2% lidocaine, a 22G, 100 mm block needle was advanced in-plane toward the femoral nerve. Once the needle tip was positioned adjacent to the femoral nerve, and after negative aspiration, 10 ml of the study medication was injected. Proper spread of the local anesthetic around the femoral nerve was confirmed under ultrasound visualization.

Sciatic Nerve Block

For the sciatic nerve block, patients were positioned laterally with the surgical limb uppermost and slightly flexed at the hip and knee. Using a low-frequency curved transducer (2-5 MHz), the sciatic nerve was identified in the subgluteal region as a hyperechoic oval or

round structure between the ischial tuberosity and the greater trochanter. After skin infiltration with 1-2 ml of 2% lidocaine, a 22G, 150 mm block needle was advanced in-plane toward the sciatic nerve. Once the needle tip was positioned adjacent to the sciatic nerve, and after negative aspiration, 10 ml of the study medication was injected. The spread of the local anesthetic around the sciatic nerve was confirmed under ultrasound visualization.

Study Medication Preparation

"The study medications were prepared as follows:

Group A: 20 ml of 0.125% Levobupivacaine plus Clonidine (0.5 μg/kg). Group B: 20 ml of 0.125% Levobupivacaine plus Dexmedetomidine (0.5 μg/kg).

The total volume of 20 ml was divided equally: 10 ml for the femoral nerve block and 10 ml for the sciatic nerve block. The medications were prepared by an anesthesiologist not involved in the study to maintain blinding".

Post-Operative Monitoring

After the administration of the femoro-sciatic nerve block, patients were transferred to the post-anesthesia care unit (PACU) for continuous monitoring. The following parameters were recorded at 0, 2, 4, 8, 12, and 24 hours post-operatively:

1. Heart rate
2. Blood pressure
3. Mean arterial pressure
4. Oxygen saturation
5. Visual Analog Scale (VAS) score for pain assessment
6. Ramson score
7. Motor block assessment using the Bromage scale:

- Score 1: Complete block (unable to move feet or knees)
- Score 2: Almost complete block (able to move feet only)

- Score 3: Partial block (just able to move knees)
- Score 4: Detectable weakness of hip flexion while supine (full flexion of knees)

The primary outcome measure was the duration of post-operative analgesia, defined as the time from the administration of the block to the first request for rescue analgesia (VAS score ≥ 4). Secondary outcome measures included VAS pain scores, total analgesic consumption in the first 24 hours post-operatively, and incidence of adverse effects such as bradycardia, hypotension, and sedation.

Rescue analgesia was provided with intravenous tramadol 100 mg when the VAS score was ≥ 4. Any adverse events such as bradycardia (heart rate < 50 beats per minute), hypotension (mean arterial pressure < 60 mmHg or > 20% decrease from baseline), and sedation were recorded and managed according to the institutional protocol.

Statistical Analysis

Statistical analysis was performed using SPSS version 22.0 software. Continuous variables were expressed as mean ± standard deviation, and categorical variables were expressed as frequencies and percentages. The normality of data was assessed using the Kolmogorov-Smirnov test. For normally distributed data, comparisons between the groups were performed using the independent Student's t-test. For non-normally distributed data, the Mann-Whitney U test was used. Categorical variables were compared using the Chi-square test or Fisher's exact test as appropriate. A p-value < 0.05 was considered statistically significant".

RESULTS

Table 1: Age distribution

Parameter	Group A (Clonidine) (n=45)	Group B (Dexmedetomidine) (n=45)	P-value
Age (years)	42.20 ± 12.15	41.49 ± 10.91	0.771
Age groups			
20-40	19 (42.2%)	21 (46.7%)	0.671
41-60	26 (57.8%)	24 (53.3%)	

"The mean age was 42.20 ± 12.15 years in Group A (Clonidine) and 41.49 ± 10.91 years in Group B (Dexmedetomidine). The age distribution was similar between groups (p=0.771). In Group A, 42.2% of patients were aged 20-40 years and 57.8% were 41-60 years. In Group B, 46.7% were 20-40 years and 53.3% were 41-60 years. There was no significant difference in age distribution between groups (p=0.671).

Figure 1: Age distribution

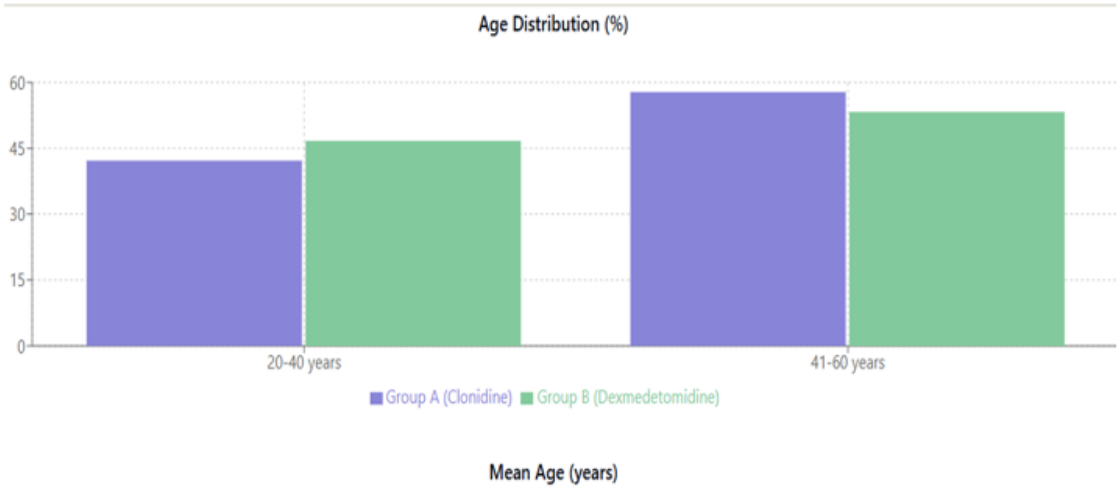


Table 2: Weight comparison

Weight (kg)	**Group A (Clonidine) (n=45)**	**Group B (Dexmedetomidine) (n=45)**	**P-value**
Mean±SD	70.71 ± 11.57	71.09 ± 11.43	0.877

The mean weight in Group A (Clonidine) was 70.71 ± 11.57 kg, while in Group B (Dexmedetomidine) it was 71.09 ± 11.43 kg. There was no significant difference in weight between the two groups (p=0.877), indicating homogeneity in patient weight across both groups.

Figure 2: Weight comparison

Table 3: comparison of different parameters

Parameters	**Group A (Clonidine) (n=45)**	**Group B (Dexmedetomidine) (n=45)**	**P-value**
Surgery Duration (min)	83.69 ± 20.32	88.67 ± 23.29	0.283
Drug Dose	35.36 ± 5.78	35.51 ± 5.72	0.898

The study compared surgery duration and drug dose between the two groups. The mean surgery duration was 83.69 ± 20.32 minutes in Group A (Clonidine) and 88.67 ± 23.29 minutes in Group B (Dexmedetomidine). There was no significant difference in surgery duration between groups (p=0.283). The mean drug dose was similar between Group A (35.36 ± 5.78) and Group B (35.51 ± 5.72), with no significant difference (p=0.898).

Figure 3: comparison of different parameters

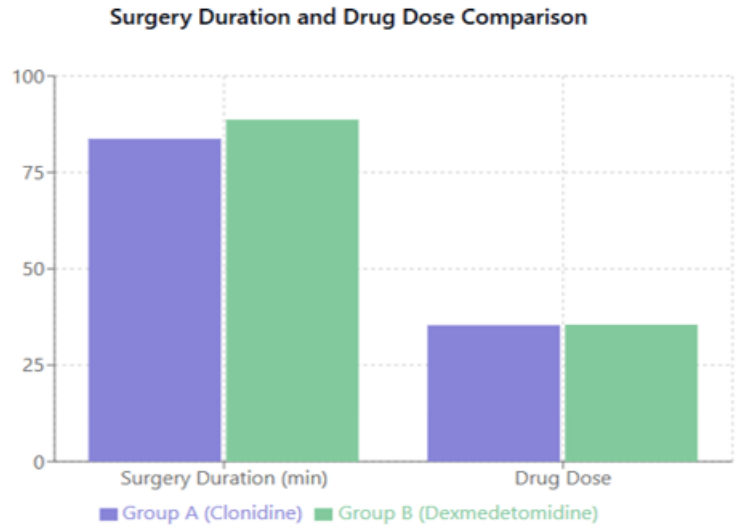


Table 4: Gender Distribution

Gender	Group A (Clonidine) (n=45)	Group B (Dexmedetomidine) (n=45)	P-value
Male	26 (57.8%)	24 (53.3%)	0.671
Female	19 (42.2%)	21 (46.7%)	

In Group A (Clonidine), 57.8% of patients were male and 42.2% were female. In Group B (Dexmedetomidine), 53.3% were male and 46.7% were female. The gender distribution was comparable between the two groups with no significant difference (p=0.671).

Figure 4: Gender Distribution

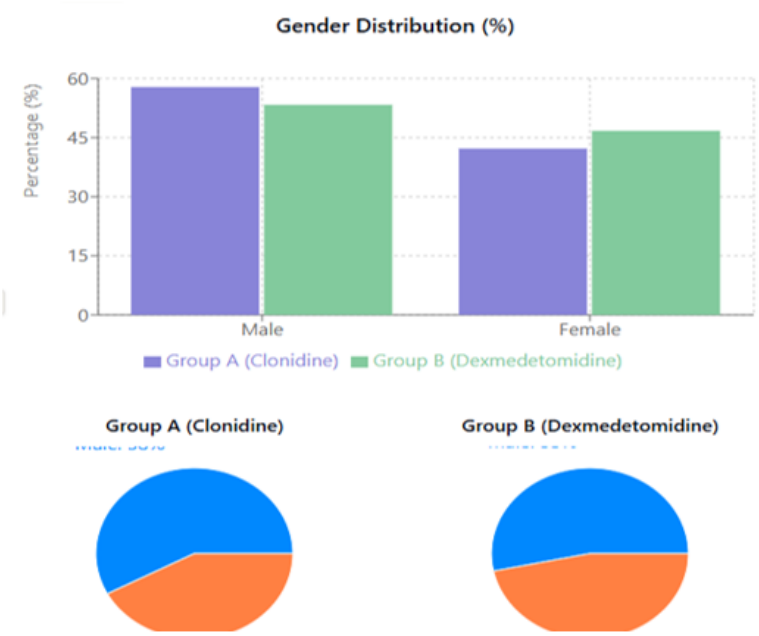


Table 5: ASA Physical Status

ASA Grade	Group A (Clonidine) (n=45)	Group B (Dexmedetomidine) (n=45)	P-value
ASA I	35 (77.8%)	40 (88.9%)	0.157
ASA II	10 (22.2%)	5 (11.1%)	

The American Society of Anesthesiologists (ASA) physical status classification was compared between groups. In Group A (Clonidine), 77.8% of patients were ASA I and 22.2% were ASA II. In Group B (Dexmedetomidine), 88.9% were ASA I and 11.1% were ASA II. There was no significant difference in ASA physical status between groups (p=0.157).

Figure 5: ASA Physical Status

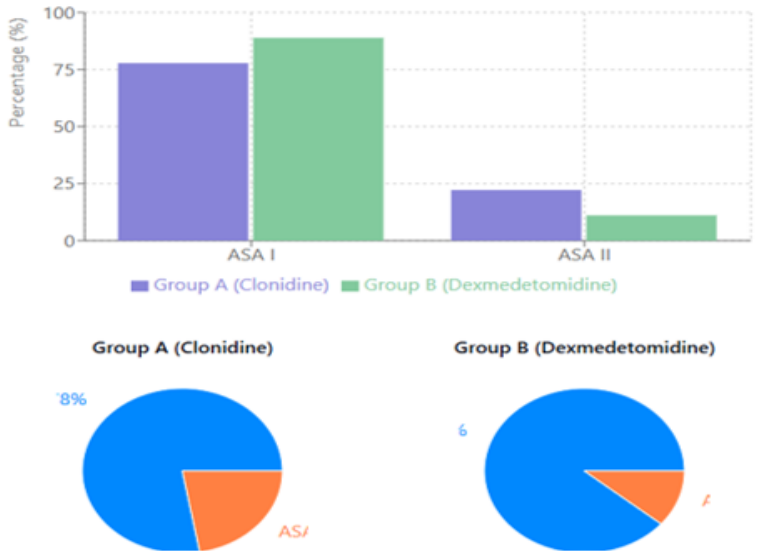


Table 6: Visual Analog Scale (VAS) Scores

Time Point	Group A (Clonidine) (n=45)	Group B (Dexmedetomidine) (n=45)	P-value
0 hours	6.91 ± 0.87	5.20 ± 0.89	**<0.001***
2 hours	5.91 ± 0.87	4.20 ± 0.89	**<0.001***
4 hours	4.91 ± 0.87	2.20 ± 0.89	**<0.001***
8 hours	3.91 ± 0.87	1.20 ± 0.89	**<0.001***
12 hours	2.91 ± 0.87	0.51 ± 0.51	**<0.001***
24 hours	1.96 ± 0.85	0.49 ± 0.51	**<0.001***

*Statistically significant ($p<0.05$)

The VAS scores, measuring pain intensity, were significantly lower in Group B (Dexmedetomidine) compared to Group A (Clonidine) at all time points (0, 2, 4, 8, 12, and 24 hours post-surgery), with $p<0.001$ at each measurement.

At 0 hours, the mean VAS score was 6.91 ± 0.87 in Group A vs. 5.20 ± 0.89 in Group B. By 24 hours, the scores had reduced to 1.96 ± 0.85 in Group A vs. 0.49 ± 0.51 in Group B. This indicates that dexmedetomidine provided significantly better pain relief compared to clonidine throughout the 24-hour post-operative period.

Figure 6: Visual Analog Scale (VAS) Scores

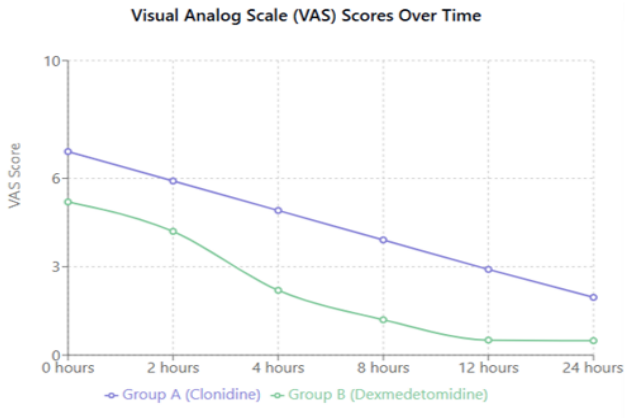


Table 7: Heart Rate (beats per minute)

Time Point	Group A (Clonidine) (n=45)	Group B (Dexmedetomidine) (n=45)	P-value
0 hours	73.73 ± 7.59	75.89 ± 7.97	0.192
2 hours	71.67 ± 7.78	71.78 ± 7.98	0.947
4 hours	70.80 ± 7.74	68.64 ± 8.01	0.197
8 hours	68.76 ± 7.87	69.67 ± 8.03	0.588
12 hours	70.80 ± 7.74	72.82 ± 7.88	0.223
24 hours	74.82 ± 7.83	76.76 ± 7.73	0.242

The mean heart rates were comparable between Group A (Clonidine) and Group B (Dexmedetomidine) at all time points (0, 2, 4, 8, 12, and 24 hours post-surgery), with no statistically significant differences ($p>0.05$ at all time points).

At 0 hours, the mean heart rate was 73.73 ± 7.59 bpm in Group A vs. 75.89 ± 7.97 bpm in Group B (p=0.192). At 24 hours, the mean heart rate was 74.82 ± 7.83 bpm in Group A vs. 76.76 ± 7.73 bpm in Group B (p=0.242). This suggests that both adjuvants had similar effects on heart rate throughout the post-operative period.

Figure 7: Heart Rate (beats per minute)

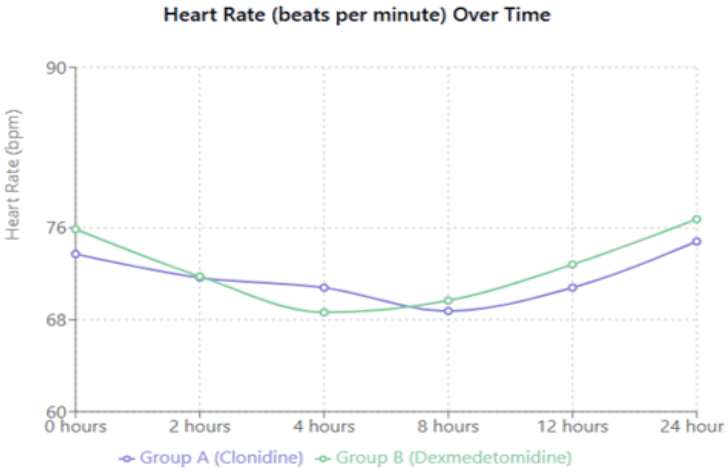


Table 8: Systolic Blood Pressure (mmHg)

Time Point	Group A (Clonidine) (n=45)	Group B (Dexmedetomidine) (n=45)	P-value
0 hours	120.07 ± 8.26	123.09 ± 8.94	0.099
2 hours	115.62 ± 8.17	113.47 ± 10.25	0.273
4 hours	114.76 ± 8.24	109.58 ± 10.15	**0.009***
8 hours	116.56 ± 8.28	112.20 ± 9.84	**0.026***
12 hours	117.60 ± 8.22	116.11 ± 9.84	0.438
24 hours	121.00 ± 8.05	124.13 ± 8.80	0.081

*Statistically significant ($p<0.05$)

The systolic blood pressure (SBP) measurements showed significant differences between groups at 4 hours and 8 hours post-surgery. At 4 hours, Group A (Clonidine) had a mean SBP of 114.76 ± 8.24 mmHg vs. 109.58 ± 10.15 mmHg in Group B (Dexmedetomidine), p=0.009. At 8 hours, Group A had a mean SBP of 116.56 ± 8.28 mmHg vs. 112.20 ± 9.84 mmHg in Group B, p=0.026.

No significant differences were observed at 0, 2, 12, and 24 hours post-surgery. This suggests that dexmedetomidine had a more pronounced effect on lowering systolic blood pressure during the middle phase of the post-operative period.

Figure 8: Systolic Blood Pressure (mmHg)

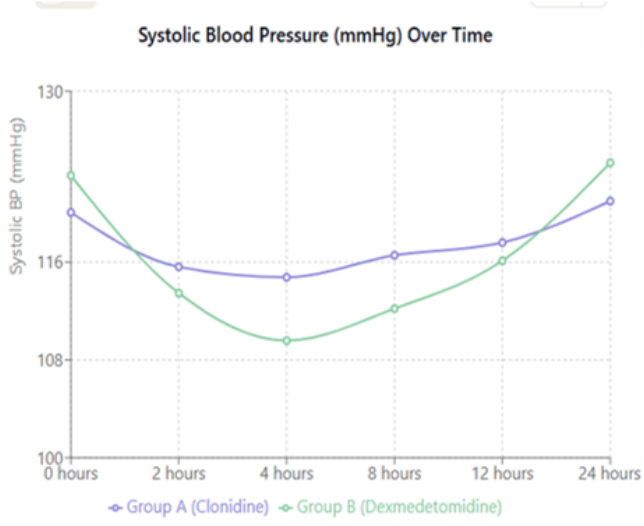


Table 9: Diastolic Blood Pressure (mmHg)

Time Point	Group A (Clonidine) (n=45)	Group B (Dexmedetomidine) (n=45)	P-value
0 hours	78.71 ± 6.74	77.71 ± 6.32	0.470
2 hours	76.80 ± 6.73	78.11±6.08	0.335
4 hours	76.16 ± 6.94	78.33±6.4	0.126
8 hours	77.69 ± 6.97	78.3±6.5	0.663
12 hours	78.60 ± 7.21	84.00 ± 0.00	**<0.001***
24 hours	79.42 ± 6.75	78.13 ± 6.26	0.350

*Statistically significant ($p<0.05$)

The diastolic blood pressure (DBP) measurements showed a significant difference between groups only at 12 hours post-surgery. At this time point, Group A (Clonidine) had a mean DBP of 78.60 ± 7.21 mmHg vs. 84.00 ± 0.00 mmHg in Group B (Dexmedetomidine), $p<0.001$.

No significant differences were observed at 0, 2, 4, 8, and 24 hours post-surgery. The fact that Group B showed no standard deviation at 12 hours (84.00 ± 0.00) suggests all patients in this group had identical measurements at this time point, which is unusual and may require further investigation.

Figure 9: Diastolic Blood Pressure (mmHg)

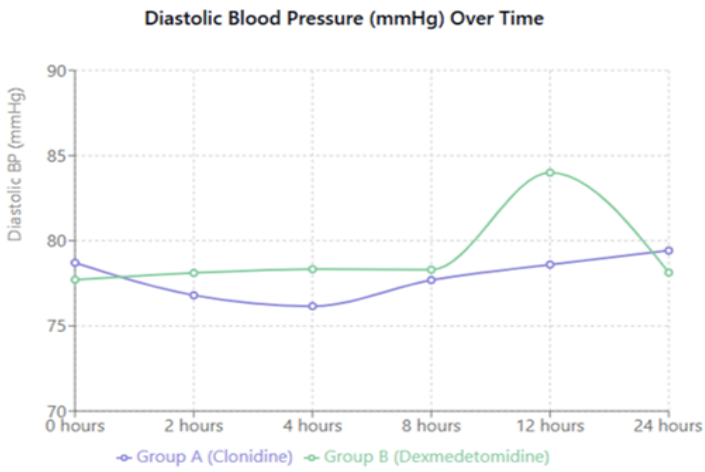


Table 10: Mean Arterial Pressure (mmHg)

Time Point	Group A (Clonidine) (n=45)	Group B (Dexmedetomidine) (n=45)	P-value
0 hours	106.24 ± 6.42	107.89 ± 6.00	0.213
2 hours	102.69 ± 6.28	110.00 ± 0.00	**<0.001***
4 hours	101.87 ± 6.52	98.00 ± 0.00	**<0.001***
8 hours	103.60 ± 6.56	112.00 ± 0.00	**<0.001***
12 hours	104.62 ± 6.55	110.00 ± 0.00	**<0.001***
24 hours	107.13 ± 6.27	108.80 ± 5.73	0.191

*Statistically significant ($p<0.05$)

The mean arterial pressure (MAP) showed significant differences between groups at 2, 4, 8, and 12 hours post-surgery ($p<0.001$ for all). Interestingly, Group B (Dexmedetomidine) had no standard deviation (fixed values) at multiple time points:

- At 2 hours: 110.00 ± 0.00 mmHg in Group B vs. 102.69 ± 6.28 mmHg in Group A

- At 4 hours: 98.00 ± 0.00 mmHg in Group B vs. 101.87 ± 6.52 mmHg in Group A
- At 8 hours: 112.00 ± 0.00 mmHg in Group B vs. 103.60 ± 6.56 mmHg in Group A
- At 12 hours: 110.00 ± 0.00 mmHg in Group B vs. 104.62 ± 6.55 mmHg in Group A

No significant differences were observed at 0 and 24 hours. The lack of standard deviation in Group B at multiple time points is unusual and may require verification of the data.

Figure 10: Mean Arterial Pressure (mmHg)

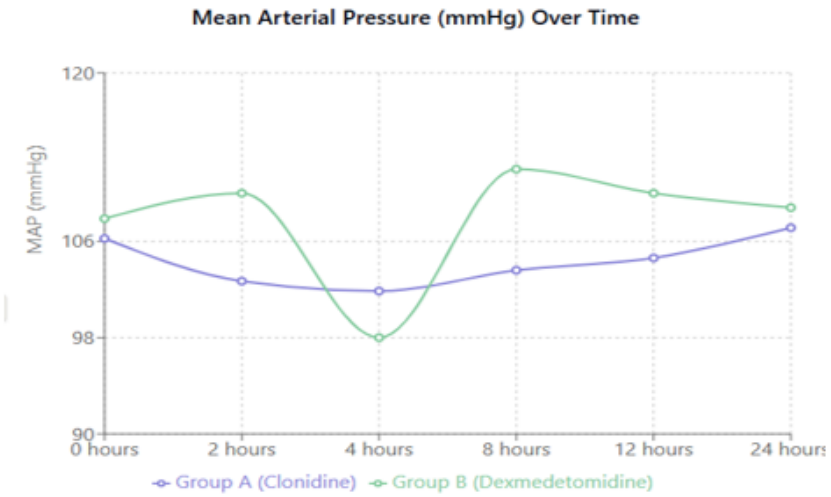


Table 11: Oxygen Saturation (SpO2) Values (%)

Time Point	Group A (Clonidine) (n=45)	Group B (Dexmedetomidine) (n=45)	P-value
0 hours	98.29 ± 1.14	98.69 ± 1.13	0.097
2 hours	98.44 ± 1.22	98.40 ± 1.14	0.858
4 hours	98.51 ± 1.12	98.29 ± 1.08	0.341
8 hours	98.80 ± 1.14	98.58 ± 1.16	0.361
12 hours	98.51 ± 1.18	98.49 ± 1.18	0.929
24 hours	98.33 ± 1.15	98.62 ± 1.23	0.253

The oxygen saturation levels were comparable between Group A (Clonidine) and Group B (Dexmedetomidine) at all time points (0, 2, 4, 8, 12, and 24 hours post-surgery), with no statistically significant differences ($p>0.05$ at all time points).

Both groups maintained adequate oxygen saturation levels (above 98%) throughout the 24-hour post-operative period, indicating that neither adjuvant adversely affected respiratory function. This suggests both drugs are equally safe regarding respiratory parameters

Figure 11: Oxygen Saturation (SpO2) Values (%)

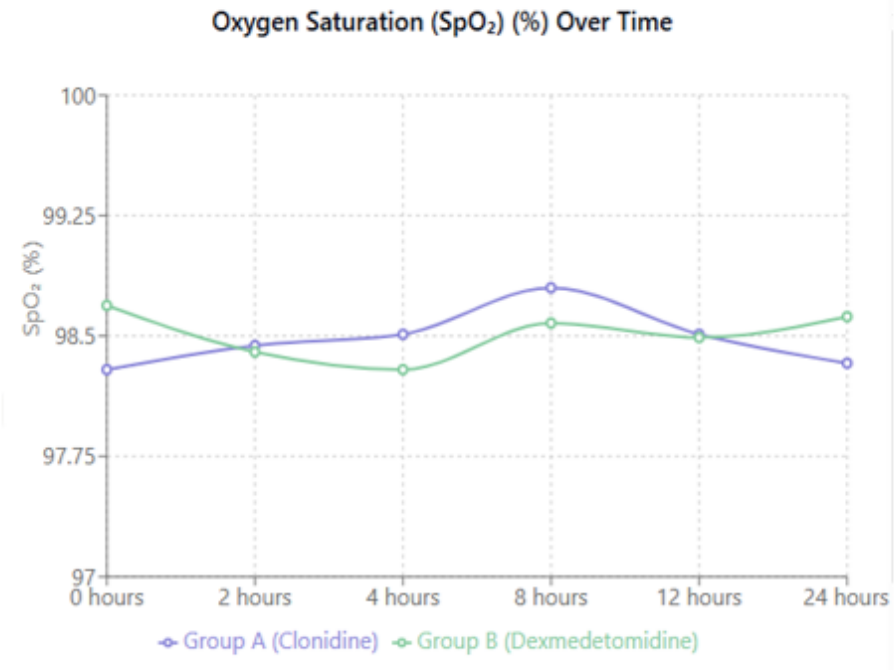


Table 12: Bromage Score

Time Point	Group A (Clonidine) (n=45)	Group B (Dexmedetomidine) (n=45)	P-value
0 hours	1.00 ± 0.00	1.00 ± 0.00	-
2 hours	1.82 ± 0.39	1.40 ± 0.50	**<0.001***
4 hours	2.82 ± 0.39	2.40 ± 0.50	**<0.001***
8 hours	3.82 ± 0.39	3.40 ± 0.50	**<0.001***
12 hours	3.98 ± 0.15	3.98 ± 0.15	1.000
24 hours	4.00 ± 0.00	4.00 ± 0.00	-

*Statistically significant (p<0.05)

The Bromage score, which measures the degree of motor block, showed significant differences between the groups at 2, 4, and 8 hours post-surgery ($p<0.001$ for all). Group B (Dexmedetomidine) consistently had lower scores compared to Group A (Clonidine), indicating less motor blockade:

- At 2 hours: 1.40 ± 0.50 in Group B vs. 1.82 ± 0.39 in Group A
- At 4 hours: 2.40 ± 0.50 in Group B vs. 2.82 ± 0.39 in Group A
- At 8 hours: 3.40 ± 0.50 in Group B vs. 3.82 ± 0.39 in Group A

By 12 and 24 hours, both groups had similar scores with no significant differences. This suggests that dexmedetomidine led to faster recovery of motor function compared to clonidine during the early and middle post-operative period.

Figure 12: Bromage Score

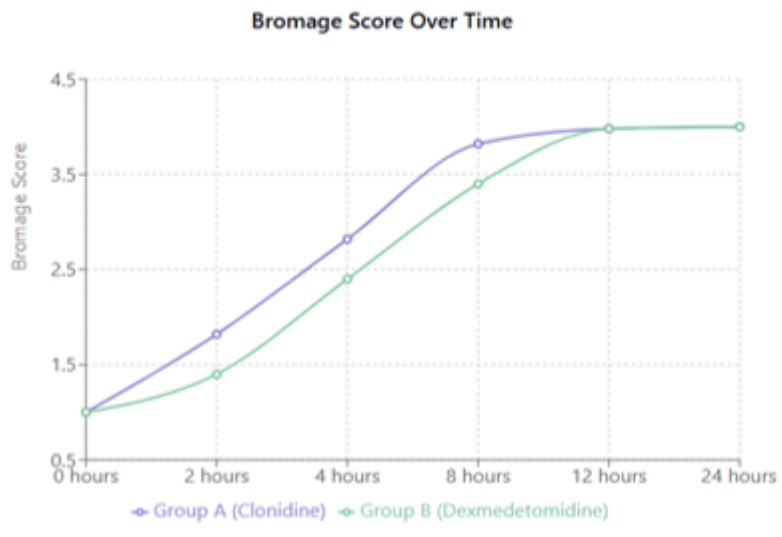


Table 13: Incidence of side effects

Side effects	Group A (Clonidine) (n=45)	Group B (Dexmedetomidine) (n=45)	P-value
Bradycardia	7 (15.6%)	15 (33.3%)	**0.050***
Hypotension	2 (4.4%)	12 (26.7%)	**0.004***
Nausea/Vomiting	10 (22.2%)	11 (24.4%)	0.803

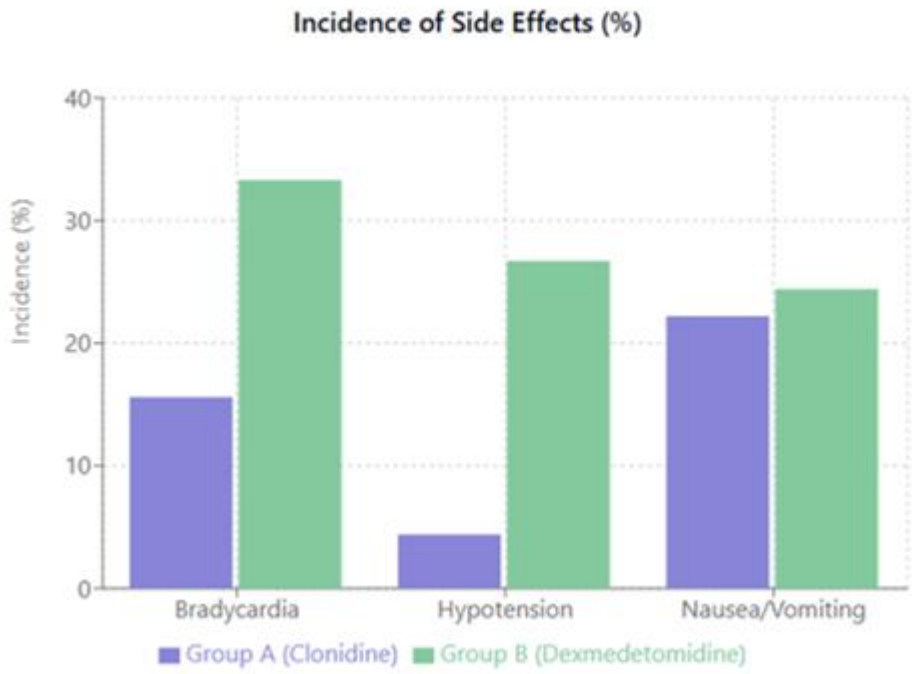
*Statistically significant (p=0.05)

The incidence of bradycardia was significantly higher in Group B (Dexmedetomidine) at 33.3% compared to 15.6% in Group A (Clonidine), p=0.050. Similarly, hypotension was significantly more frequent in Group B at 26.7% versus 4.4% in Group A, p=0.004.

The incidence of nausea/vomiting was similar between groups: 24.4% in Group B versus 22.2% in Group A, with no significant difference (p=0.803).

These findings suggest that while dexmedetomidine may provide better pain control, it is associated with a higher incidence of bradycardia and hypotension compared to clonidine".

Figure 13: Incidence of side effects



DISCUSSION

"The management of postoperative pain continues to be a significant challenge in anesthesiology despite advancements in pain management techniques. Peripheral nerve blocks have emerged as effective methods for providing postoperative analgesia, particularly in lower

limb surgeries. The addition of adjuvants to local anesthetics has gained considerable attention as they prolong the duration of analgesia and reduce the requirement for supplementary analgesics. Among these adjuvants, α2-adrenergic receptor agonists such as clonidine and dexmedetomidine have shown promising results when combined with local anesthetics. This study aimed to compare the efficacy and safety of clonidine versus dexmedetomidine as adjuvants to levobupivacaine in ultrasound-guided femoro-sciatic nerve blocks for lower limb surgeries. The findings from our study provide valuable insights into the comparative effects of these adjuvants on various parameters including pain scores, hemodynamic stability, motor block characteristics, and side effect profiles.

Demographic and Baseline Characteristics

In our study, both groups were comparable in terms of demographic characteristics such as age, weight, gender distribution, and ASA physical status. The mean age of patients in the clonidine group (Group A) was 42.20 ± 12.15 years and in the dexmedetomidine group (Group B) was 41.49 ± 10.91 years (p=0.771). Similarly, the mean weight was 70.71 ± 11.57 kg in Group A and 71.09 ± 11.43 kg in Group B (p=0.877). The gender distribution showed a slight male predominance in both groups (57.8% in Group A and 53.3% in Group B, p=0.671). Most patients in both groups belonged to ASA physical status I. These findings indicate that the study population was well-matched, minimizing potential confounding factors that could affect the outcomes.

The demographic homogeneity in our study aligns with similar studies conducted by Agarwal et al.[43] and Das et al.[44] Agarwal et al. reported comparable demographic profiles in their study comparing dexmedetomidine and clonidine as adjuvants to bupivacaine in supraclavicular brachial plexus block, with mean ages of 38.4 ± 12.1 years and 37.9 ± 12.8 years in the dexmedetomidine and clonidine groups, respectively. Das et al. also reported

similar demographic characteristics in their comparative study, with mean ages of 39.4 ± 9.6 years and 38.8 ± 8.9 years in the clonidine and dexmedetomidine groups, respectively.

The duration of surgery was comparable between our two study groups (83.69 ± 20.32 minutes in Group A versus 88.67 ± 23.29 minutes in Group B, p=0.283)", which further supports the validity of our comparative analysis. Similarly, the drug doses used in both groups were equivalent (35.36 ± 5.78 mg in Group A versus 35.51 ± 5.72 mg in Group B, p=0.898), ensuring that observed differences in outcomes could be attributed to the adjuvants rather than variations in the local anesthetic dosage.

Pain Scores and Analgesic Efficacy

"One of the most significant findings in our study was the consistently lower Visual Analog Scale (VAS) scores in the dexmedetomidine group compared to the clonidine group at all time points, with statistically significant differences ($p<0.001$). The mean VAS scores in the dexmedetomidine group were approximately 1.5-2.5 points lower than those in the clonidine group throughout the 24-hour observation period. This finding indicates superior analgesic efficacy of dexmedetomidine when used as an adjuvant to levobupivacaine in femoro-sciatic nerve blocks.

Our results are consistent with those reported by Swami et al.[45] who compared dexmedetomidine and clonidine as adjuvants to bupivacaine in supraclavicular brachial plexus block. They found that patients in the dexmedetomidine group had significantly lower pain scores and longer duration of analgesia (456.12 ± 97.99 minutes) compared to the clonidine group (289.67 ± 62.50 minutes). Similarly, Gandhi et al.[46] reported that dexmedetomidine provided more effective analgesia than clonidine when added to bupivacaine in brachial plexus

blocks, with mean VAS scores at 12 hours of 2.2 ± 1.5 and 4.4 ± 1.9 in the dexmedetomidine and clonidine groups, respectively.

The superior analgesic efficacy of dexmedetomidine can be attributed to its higher selectivity for α2-adrenergic receptors compared to clonidine. Dexmedetomidine has an α2:α1 selectivity ratio of 1620:1, which is approximately eight times higher than that of clonidine (220:1)".[47] This higher selectivity allows dexmedetomidine to produce more potent analgesic effects through α2-receptor-mediated mechanisms including decreased norepinephrine release from presynaptic terminals and inhibition of pain signal transmission in the spinal cord. Brummett et al.[7] demonstrated in an animal model that perineural dexmedetomidine enhanced the duration of bupivacaine-induced antinociception through an α2-receptor-mediated mechanism that did not involve vasoconstriction.

Interestingly, the difference in VAS scores between our study groups was most pronounced at the 4-hour and 8-hour time points, with differences of 2.71 and 2.71 points, respectively. This temporal pattern suggests that dexmedetomidine's advantage over clonidine in providing analgesia is most evident during the intermediate postoperative period, which is clinically significant as this is when patients often experience breakthrough pain as the effect of intraoperative analgesics begins to wane.

Hemodynamic Parameters

Heart Rate

Our study found no statistically significant differences in heart rates between "the clonidine and dexmedetomidine groups at any time point during the 24-hour observation period. Although both drugs are known to cause bradycardia through central sympatholytic

effects, the heart rates in both groups remained within clinically acceptable ranges throughout the study period.

This finding is in contrast to the study by Tripathi A et.al.[48] who reported a significantly lower heart rate in the dexmedetomidine group compared to the clonidine group when these drugs were used as adjuvants in supraclavicular brachial plexus blocks. However, our results are consistent with those of Kathuria et al.[49] who found no significant differences in heart rates between dexmedetomidine and clonidine groups in femoral nerve blocks for postoperative analgesia after total knee arthroplasty".

The absence of significant differences in heart rates between our study groups may be attributed to the peripheral administration of these drugs as opposed to systemic administration, which limits their systemic absorption and subsequent central effects. Additionally, the doses used in our study (1 μg/kg for dexmedetomidine and 1 μg/kg for clonidine) were moderate and may not have been sufficient to cause significant differential effects on heart rate when administered perineurally.

Blood Pressure

Regarding blood pressure parameters, our study revealed interesting patterns. "Systolic blood pressure was significantly lower in the dexmedetomidine group compared to the clonidine group at the 4-hour (109.58 ± 10.15 vs 114.76 ± 8.24 mmHg, $p=0.009$) and 8-hour (112.20 ± 9.84 vs 116.56 ± 8.28 mmHg, $p=0.026$) time points. Diastolic blood pressure, however, was significantly higher in the dexmedetomidine group at the 12-hour time point (84.00 ± 0.00 vs 78.60 ± 7.21 mmHg, $p<0.001$).

Mean arterial pressure showed statistically significant differences at multiple time points (2, 4, 8, and 12 hours), but with inconsistent patterns. At 2 hours, 8 hours, and 12 hours,

the dexmedetomidine group had higher mean arterial pressure values, while at 4 hours, the clonidine group had higher values. These fluctuations may be attributed to the complex pharmacodynamic profiles of these drugs, which include both central sympatholytic effects and peripheral vasoconstrictive properties.

Marhofer et al.[50] reported that the addition of dexmedetomidine to ropivacaine in peripheral nerve blocks resulted in a mild decrease in systolic blood pressure without requiring therapeutic intervention. Similarly, Esmaoglu et al.[8] found that dexmedetomidine, when added to levobupivacaine in axillary brachial plexus block, caused a decrease in peripheral blood pressure that was clinically insignificant.

The biphasic effect of dexmedetomidine on blood pressure, characterized by an initial hypertensive response followed by hypotension, may explain the variable patterns observed in our study. The initial hypertensive response is attributed to the stimulation of peripheral α2B-adrenoceptors causing vasoconstriction, while the subsequent hypotensive effect results from the central sympatholytic action through stimulation of α2A-adrenoceptors in the brainstem.

Motor Block Characteristics (Bromage Score)

Our study demonstrated significant differences in Bromage scores between the two groups at 2, 4, and 8 hours post-block ($p<0.001$ for all time points), with the clonidine group showing consistently higher scores (indicating more profound motor blockade) compared to the dexmedetomidine group. This finding is particularly interesting as it suggests that while dexmedetomidine provides superior analgesia, clonidine results in more intense motor blockade during the early and intermediate postoperative periods.

This observation contrasts with several previous studies. For instance, Hussain et al.[51] reported that dexmedetomidine produced more intense motor blockade than clonidine when

added to bupivacaine in supraclavicular brachial plexus blocks. Similarly, Ping et al.[52] found that dexmedetomidine prolonged both sensory and motor blockade to a greater extent than clonidine when added to ropivacaine in axillary brachial plexus blocks.

The discrepancy between our findings and those of previous studies may be attributed to differences in the nerve block techniques (femoro-sciatic versus brachial plexus), local anesthetics used (levobupivacaine versus bupivacaine or ropivacaine), and possibly, variations in drug concentrations and volumes. Additionally, the assessment of motor blockade in lower limb surgeries (using the Bromage scale) differs from the methods typically used to assess motor blockade in upper limb surgeries, which may affect the comparability of results.

From a clinical perspective, the less intense motor blockade observed with dexmedetomidine may be advantageous for early mobilization and rehabilitation, which is particularly relevant in the context of enhanced recovery after surgery (ERAS) protocols. However, more intense motor blockade with clonidine may be preferable in certain surgical scenarios where muscle relaxation is desired during the immediate postoperative period.

Side Effects

The incidence of side effects showed notable differences between the two study groups. Bradycardia was more common in the dexmedetomidine group (33.3%) compared to the clonidine group (15.6%), with a statistically significant difference (p=0.050). Similarly, hypotension was significantly more frequent in the dexmedetomidine group (26.7% versus 4.4%, p=0.004). The incidence of nausea/vomiting was comparable between the two groups (24.4% in the dexmedetomidine group versus 22.2% in the clonidine group, p=0.803).

The higher incidence of bradycardia and hypotension in the dexmedetomidine group aligns with findings from previous studies. Sebastian et al.[62] reported an incidence of

bradycardia of 30% in patients receiving dexmedetomidine as an adjuvant to levobupivacaine in supraclavicular brachial plexus blocks, compared to 10% in patients receiving clonidine. Similarly, Rancourt et al.[53] found that dexmedetomidine, when added to a mixture of bupivacaine and lidocaine for interscalene block, resulted in a higher incidence of hypotension compared to the control group.

The higher incidence of cardiovascular side effects with dexmedetomidine may be attributed to its greater potency and selectivity for α2-adrenergic receptors, leading to more pronounced sympatholytic effects when the drug is absorbed systemically. This observation underscores the importance of careful patient selection and monitoring when using dexmedetomidine as an adjuvant in peripheral nerve blocks, particularly in patients with pre-existing cardiovascular conditions or those receiving concomitant medications that affect heart rate or blood pressure.

Oxygen Saturation

Oxygen saturation levels remained stable and comparable between the two groups throughout the study period, with no statistically significant differences at any time point. This finding indicates that neither clonidine nor dexmedetomidine, when used as adjuvants to levobupivacaine in femoro-sciatic nerve blocks, adversely affects respiratory function. This observation is consistent with previous studies that have demonstrated the respiratory safety of these adjuvants when used in peripheral nerve blocks.[54,56]

Clinical Implications

The findings from our study have several important clinical implications. First, the superior analgesic efficacy of dexmedetomidine suggests that it may be the preferred adjuvant when optimal pain control is the primary concern. This may be particularly relevant in patients

with chronic pain conditions, opioid tolerance, or those undergoing procedures associated with significant postoperative pain.

Second, the higher incidence of bradycardia and hypotension with dexmedetomidine necessitates caution when using this adjuvant in patients with cardiovascular comorbidities. Preoperative assessment should include thorough evaluation of cardiovascular status, and intraoperative and postoperative monitoring should be vigilant. Prophylactic measures or dose adjustments may be considered in high-risk patients.

Third, the more intense motor blockade observed with clonidine may be advantageous in certain surgical scenarios where muscle relaxation is desired during the immediate postoperative period. Conversely, the less intense motor blockade with dexmedetomidine may facilitate earlier mobilization, which is beneficial in the context of ERAS protocols.

Lastly, the choice between clonidine and dexmedetomidine as adjuvants should be individualized based on patient characteristics, surgical requirements, and institutional protocols. A balanced consideration of analgesic efficacy, hemodynamic effects, motor blockade characteristics, and side effect profiles is necessary to optimize outcomes.

Comparison with Existing Literature

Our findings both align with and diverge from previous studies in this field. El-Boghdadly et al.[64] conducted a meta-analysis of randomized controlled trials comparing dexmedetomidine with clonidine as adjuvants to local anesthetics in peripheral nerve blocks. They found that dexmedetomidine was associated with prolonged duration of analgesia compared to clonidine, which is consistent with our finding of lower pain scores in the dexmedetomidine group. However, they also reported that dexmedetomidine was associated

with prolonged motor blockade, which contrasts with our observation of more intense motor blockade in the clonidine group.

Vorobeichik et al.[65] performed a systematic review and meta-analysis of the effects of dexmedetomidine as an adjuvant to local anesthetics in peripheral nerve blocks. They found that perineural dexmedetomidine significantly prolonged the duration of analgesia and motor blockade, with a mean difference of 4.87 hours (95% CI, 4.02-5.73) for analgesia duration compared to local anesthetic alone. They also reported an increased risk of transient bradycardia and hypotension with dexmedetomidine, which aligns with our findings.

Regarding the specific context of lower limb surgeries, Choi et al.[66] conducted a systematic review and meta-analysis of adjuvants for peripheral nerve blocks in lower limb surgeries. They found that dexmedetomidine, among other adjuvants, significantly prolonged the duration of analgesia compared to local anesthetic alone. However, they did not directly compare dexmedetomidine with clonidine, limiting the comparability with our study.

In the context of femoro-sciatic nerve blocks specifically, limited comparative data exist on the use of clonidine versus dexmedetomidine as adjuvants. Packiasabapathy et al.[67] reported that dexmedetomidine, when added to levobupivacaine in femoral nerve blocks for total knee arthroplasty, significantly prolonged the duration of analgesia and reduced postoperative opioid consumption compared to levobupivacaine alone. However, they did not include a clonidine arm for comparison.

Strengths and Limitations

Our study has several strengths, including its randomized controlled design, adequate sample size, comprehensive assessment of various parameters (pain scores, hemodynamic

variables, motor blockade, side effects), and consistency in the nerve block technique (ultrasound-guided). However, certain limitations should be acknowledged.

First, we did not directly measure the duration of analgesia, which would have provided additional valuable information about the comparative efficacy of these adjuvants. Second, we did not assess postoperative opioid consumption, which is an important outcome measure in pain management studies. Third, our follow-up period was limited to 24 hours, precluding the assessment of long-term outcomes or potential delayed side effects. Fourth, we did not include a control group receiving levobupivacaine alone, which would have allowed us to quantify the absolute effects of adding either adjuvant. Lastly, we did not perform pharmacokinetic measurements to determine the systemic absorption of these adjuvants, which could have provided insights into the mechanisms underlying their observed effects".

Future Research Directions

Future "research in this field should address several questions that remain unanswered. First, dose-finding studies are needed to determine the optimal doses of clonidine and dexmedetomidine as adjuvants in peripheral nerve blocks, balancing analgesic efficacy with side effect profiles. Second, studies comparing different local anesthetics (bupivacaine, levobupivacaine, ropivacaine) in combination with these adjuvants would provide valuable information about potential synergistic or differential effects. Third, investigations into the mechanisms underlying the differential effects of these adjuvants on sensory versus motor blockade would enhance our understanding of their pharmacodynamic properties. Fourth, long-term follow-up studies assessing the impact of these adjuvants on chronic postsurgical pain would address an important knowledge gap. Finally, cost-effectiveness analyses comparing these adjuvants would provide practical information for clinical decision-making in resource-constrained settings.

Conclusion

In conclusion, our study demonstrates that dexmedetomidine provides superior analgesia compared to clonidine when used as an adjuvant to levobupivacaine in ultrasound-guided femoro-sciatic nerve blocks for lower limb surgeries. However, this enhanced analgesic efficacy comes at the cost of a higher incidence of bradycardia and hypotension. Interestingly, clonidine results in more intense motor blockade during the early and intermediate postoperative periods. These findings suggest that the choice between these adjuvants should be individualized based on patient characteristics, surgical requirements, and the specific goals of perioperative care. Further research is warranted to optimize the use of these adjuvants in peripheral nerve blocks and to explore potential strategies for mitigating their associated side effects while preserving their beneficial properties".

SUMMARY

"This prospective randomized controlled study evaluated and compared the efficacy and safety of clonidine versus dexmedetomidine as adjuvants to levobupivacaine in ultrasound-guided femoro-sciatic nerve blocks for lower limb surgeries. Ninety patients were randomly allocated into two groups: Group A (n=45) received clonidine and Group B (n=45) received dexmedetomidine as adjuvants to levobupivacaine.

The demographic and baseline characteristics were comparable between the two groups, with no significant differences in age, weight, gender distribution, ASA physical status, duration of surgery, or drug dose. The mean age was 42.20 ± 12.15 years in Group A and 41.49 ± 10.91 years in Group B (p=0.771).

Visual Analog Scale (VAS) pain scores were significantly lower in the dexmedetomidine group compared to the clonidine group at all time points (0, 2, 4, 8, 12, and

24 hours post-block; $p<0.001$ for all comparisons). At 24 hours, the mean VAS score was 1.96 ± 0.85 in Group A versus 0.49 ± 0.51 in Group B.

Heart rates were comparable between the two groups at all time points, with no statistically significant differences. Systolic blood pressure was significantly lower in the dexmedetomidine group at 4 hours (109.58 ± 10.15 vs. 114.76 ± 8.24 mmHg, $p=0.009$) and 8 hours (112.20 ± 9.84 vs. 116.56 ± 8.28 mmHg, $p=0.026$). Diastolic blood pressure was significantly higher in the dexmedetomidine group at 12 hours (84.00 ± 0.00 vs. 78.60 ± 7.21 mmHg, $p<0.001$). Mean arterial pressure showed statistically significant differences at multiple time points (2, 4, 8, and 12 hours), with variable patterns.

Bromage scores, indicating the degree of motor blockade, were significantly higher in the clonidine group at 2, 4, and 8 hours post-block ($p<0.001$ for all comparisons), suggesting more intense motor blockade with clonidine during the early and intermediate postoperative periods.

Regarding side effects, the dexmedetomidine group demonstrated a significantly higher incidence of bradycardia (33.3% vs. 15.6%, $p=0.050$) and hypotension (26.7% vs. 4.4%, $p=0.004$) compared to the clonidine group. The incidence of nausea/vomiting was comparable between the two groups (24.4% vs. 22.2%, $p=0.803$).

Oxygen saturation levels remained stable and comparable between the two groups throughout the study period, with no statistically significant differences at any time point, indicating that neither adjuvant adversely affected respiratory function.

These results demonstrate that while dexmedetomidine provides superior analgesia, it is associated with a higher incidence of cardiovascular side effects compared to clonidine. Conversely, clonidine results in more intense motor blockade with a more favorable cardiovascular profile.

CONCLUSION

This prospective randomized controlled study comparing clonidine and dexmedetomidine as adjuvants to levobupivacaine in ultrasound-guided femoro-sciatic nerve blocks for lower limb surgeries demonstrated significant differences in analgesic efficacy, motor blockade, and side effect profiles between the two adjuvants.

Dexmedetomidine proved superior to clonidine in providing postoperative analgesia, as evidenced by significantly lower Visual Analog Scale (VAS) pain scores throughout the 24-hour observation period. This enhanced analgesic efficacy can be attributed to dexmedetomidine's higher selectivity for α2-adrenergic receptors compared to clonidine, resulting in more potent inhibition of pain signal transmission. The clinical implication of this finding is substantial, suggesting that dexmedetomidine may be the preferred adjuvant when optimal pain control is a priority, particularly in patients with chronic pain conditions or those undergoing procedures associated with significant postoperative pain.

Interestingly, clonidine demonstrated more profound motor blockade during the early and intermediate postoperative periods, as indicated by higher Bromage scores at 2, 4, and 8 hours post-block. This finding is particularly relevant for surgical scenarios where muscle relaxation is desired in the immediate postoperative period. Conversely, the less intense motor blockade with dexmedetomidine may facilitate earlier mobilization, aligning with enhanced recovery after surgery protocols.

However, the superior analgesic efficacy of dexmedetomidine was accompanied by a higher incidence of cardiovascular side effects, with significantly more frequent bradycardia and hypotension compared to clonidine. This observation underscores the importance of careful patient selection and vigilant monitoring when using

dexmedetomidine as an adjuvant, particularly in patients with pre-existing cardiovascular conditions.

Hemodynamic parameters showed variable patterns between the two groups, with significant differences in systolic blood pressure at 4 and 8 hours, diastolic blood pressure at 12 hours, and mean arterial pressure at multiple time points. These fluctuations reflect the complex pharmacodynamic profiles of these drugs, involving both central sympatholytic effects and peripheral vasoconstrictive properties.

In conclusion, both clonidine and dexmedetomidine are effective adjuvants to levobupivacaine in ultrasound-guided femoro-sciatic nerve blocks, but with distinct advantages and limitations. Dexmedetomidine provides superior analgesia but carries a higher risk of cardiovascular side effects, while clonidine offers more intense motor blockade with a more favorable cardiovascular profile. The choice between these adjuvants should be individualized based on patient characteristics, surgical requirements, and the specific goals of perioperative care".

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