Bupivacaine Liposome Injectable Solutions

for Total Knee Arthroplasty Patients

Paul Halfman, CST

Post-surgically, many patients who are recovering from total knee arthroplasty (TKA) may suffer from quadriceps weakness due to a femoral nerve block they may have received preoperatively. This weakness may delay their ability to participate in physical therapy as they are unable to actively extend their leg. The administration of a long-lasting local anesthetic such as a bupivacaine liposome injectable solution at the close of the procedure in the surgical wound has recently been used in conjunction with and, in some cases, in place of a femoral nerve block in the hope of eliminating this adverse effect while maintaining adequate analgesia.

Femoral Nerve Block

A femoral nerve block is a short-term local analgesic/anesthetic administered to the femoral nerve which is the largest nerve from the lumbar plexus. The nerve originates at the second, third and fourth lumbar nerves and descends through the psoas muscle. It eventually transverses below the inguinal ligament and into the thigh. The femoral nerve supplies the muscular branches of the iliacus, pectineus, the muscles of the anterior thigh and the articular branches of the knee and hip. Examples of the pharmaceutical agents typically used for the block are lidocaine, bupivacaine, mepivacaine and ropivacaine which act as sodium channel blockers. Onset and durations vary. For example, lidocaine has a rapid onset but a shorter duration than bupivacaine. All of these injections may be prepackaged with or without epinephrine.

The blockade results in the anesthesia of the muscles of the anterior thigh and knee joint. It is performed at the inguinal crease typically with the aid of ultrasound and a peripheral nerve stimulator.
Stimulation of the nerve variably occurs at a depth of 2 to 4 cm depending upon the size of the patient. Once the nerve is visualized and an initial stimulation is obtained the current is reduced from 1.0 mA until the twitches of the quadriceps muscle disappear around 0.2 to 0.4 mA. If stimulation occurs below this level then the needle may be in the nerve itself and must be retracted as injection must occur around the nerve and not in it. After a negative aspiration to ensure the needle is not in a blood vessel the local anesthetic is injected around the femoral nerve incrementally, and in result the patient will feel dull pressure. If sharp pain is experienced, the needle may be in the nerve and must be retracted.

If a femoral nerve block is used in conjunction with the bupivacaine liposome injectable solution then non-bupivacaine based local analgesics must not be used as this creates the possibility of the immediate release of bupivacaine from the liposome. The block is typically administered by an anesthesia care provider with the assistance of a physician, PA, SA or nurse and the onset will be fairly immediate. The duration varies depending upon the agents used, the concentration and the rate at which the patient metabolizes them.

As with any nerve block a benefit is the reduced amount of systemic opiate necessary for successful anesthesia and their side effects. This is important for those patients with comorbid conditions such as obesity and respiratory disease that lead to negative effects of opioid administration/therapy. The main disadvantage of a femoral nerve block is quadriceps muscle weakness. Patients must be advised prior to consent that they will need assistance moving postoperatively for up to 24 hours and not to attempt to move independently as they will be a fall risk. They may also require the use of a knee immobilizer until they are successfully able to perform a straight-leg raise. Analgesic alternatives to the single shot femoral nerve block include techniques such as a continuous infusion femoral nerve catheter and an adductor canal block.

**BUPIVACAINE LIPOSOME INJECTABLE SOLUTION**

A bupivacaine liposome is a way to describe a molecule of bupivacaine that is packaged in a liposome “bubble.” The bupivacaine, which acts as a local analgesic, is released slowly and gradually from the bubble as it is metabolized by the body. Non-bupivacaine based local anesthetics cannot be used in conjunction with the liposomal bupivacaine as this causes an immediate release of the bupivacaine that is bound to the liposome. If a non-bupivacaine agent, such as lidocaine, has been administered prior to the liposomal bupivacaine injection (such as in a nerve block), a waiting period must be observed based on the local anesthetic used. The liposome solution is injected directly into the surgical wound including the joint capsule at the closing of the procedure.

The onset of the drug is approximately eight hours as the liposome is degraded and the bupivacaine is released. With this in mind, some surgeons may opt to use a block in conjunction with the liposomal bupivacaine to provide immediate pain relief. Another option is to include a faster acting analgesic with the injection such as bupivacaine hydrochloride.

The main benefit of the liposomal delivery system is that a single intraoperative injection can have an analgesic effect for as long as 72 hours as the membrane is metabolized.

**THE BUBBLE**

A liposome is a lipid membrane that has self-assembled into a spherical vessel. It can be comprised of single or multiple layers. Engineered liposomes can be constructed to contain items such as drugs or genetic material in their lumen or even within the layers of its shell. They can also be designed to have molecules such as proteins inserted into their membranes that will target specific areas of the body.

The main benefit of the liposomal delivery system is that a single intraoperative injection can have an analgesic effect for as long as 72 hours as the membrane is metabolized. Although it can be used in conjunction with a femoral nerve block, liposomal-based bupivacaine can be used independently potentially negating the need for a block and its adverse effects. Postoperative pain management prior to the onset of the bupivacaine liposome must be addressed by other means as onset may take eight hours. Ultimately, the liposome injectable has the potential to allow patients to begin physical therapy sooner.
TOTAL KNEE ARTHROPLASTY

A total knee arthroplasty is typically performed to correct osteoarthritis of the articular surfaces of the femur, tibia and patella. The following describes the procedure in general terms using a minimally invasive technique. Many of the instruments used are system specific and, in some cases, proprietary. This article will use basic descriptors and focus mainly on the process itself.

After a spinal block has typically been performed by the anesthesia care provider, the patient is placed in the supine position, a urinary catheter may be inserted and a tourniquet is placed proximally around the thigh. If it is applied too tightly prior to exsanguination and inflation a condition known as a venous tourniquet is created in which blood is retained within the limb. This can be avoided by fitting the cuff snugly and allowing for two fingers to fit beneath it. Once this is complete, the leg is prepped and a waiting period is observed with respect to the prep solution used. The patient is draped, a time out is taken and the leg is exsanguinated with an esmarch bandage and the tourniquet is inflated.

A longitudinal incision is created over the medial edge of the patella running superiorly from the quadriceps tendon inferiorly to the tibial tuberosity with a #10 scalpel on a #3 knife handle. The knee is flexed and the joint capsule is incised medial to the patella with a Bovie pencil or knife as sharp rakes are employed to expose the area and provide counter traction for dissection. Once this is completed, the rakes are removed and lateral retractors of various styles are used to shift the patella laterally and expose the distal articulating surface of the femur.

A large drill bit is used to create an opening into the femoral canal where an intramedullary distal femoral cutting guide is inserted and secured with screws. A large sagittal saw will cut the distal femur perpendicularly to its length. Once this is complete the guide is removed and the retractors are repositioned to the tibia. An extramedullary or intramedullary tibial cutting guide is positioned to create a cut across the proximal portion of the tibia similar to the cut in the femur. After the angle and the depth of the cut is satisfactory to the surgeon, the guide is secured with screws and the cut is made. At completion, the guide is removed along with the remaining bone debris. The menisci and any hyperplastic synovium is also removed at this point with a Kocher clamp and Bovie or knife. The leg may be placed in extension for this portion of the procedure.

After these basic cuts are completed, the femur must subsequently be sized for an implant. While in flexion, a gauge is applied on the distal femoral surface to determine the size of the cutting block that will create the anterior, posterior and diagonal chamfer cuts. Once this is determined a cutting block is locked into position with screws, retractors are inserted to protect the collateral ligaments and soft tissue, and the sagittal saw completes the shaping of the femur. The guide is removed and the trial implants are prepared.

It is extremely important to note that during this entire process the first scrub must keep track of all the settings of the cutting brackets and guides as they determine not only the size and laterality of the implants, but also the style of the implant to be used. For example, with respect to the tibia, a posteriorly stabilized implant may require a 3-degree anterior/posterior tibia angle while a cruciate retaining implant typically requires a 7-degree cutting block. Another example, in some systems the femur cuts can be referenced from the anterior or the posterior aspects and there are cutting blocks specific to both approaches.

The tibia usually receives the first trial implant. The flat, oval shaped, component rests on the proximal tibial plateau and is secured with screws. It must fit within the boundary of the surface without overhang. A rongeur can be used to remove any osteophytes around the edges of the trial implant. Next, a trial femoral implant is placed into position. A third trial component is a polyethylene insert which fixes into the tibial plate and glides along the surface of the femoral implant as the leg moves from extension to flexion. These inserts come in various thicknesses.

Lastly, the patella is prepared to receive a trial implant. The anterior/posterior thickness of the bone is measured, and the posterior aspect of the patella is removed with a sagittal saw. This can be accomplished through the use of

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a cutting guide or by freehand. Once this is complete, the diameter of the patella is determined and a drill guide is clamped into position. This guide creates holes in the posterior aspect of the patella which match the posts on the anterior aspect of the patellar implant.

After all of the trial implants are in position the surgeon will check the leg for stability and range of motion. Once these diagnostics are deemed satisfactory, all the trials are removed and the knee is ready to receive the final implants. These either can be cemented into position, press-fit or a combination of both.

The liposome injectable solution should be injected into the posterior portion of the joint capsule at this point prior to the insertion of the final polyethylene implant. It is important to avoid injecting directly into any vascular structures and the peroneal nerve and only injected into tissue where it will be retained. Injecting intra-articularly also must be avoided especially if a reinfusion drain will be used. At this time it is unknown if the bupivacaine concentration is broken down to levels low enough to safely transfuse the patient with their own drain output. Any remaining solution can be injected after the fascial layer is closed into the subcutaneous layer prior to the closing of the skin. A 20- or 22-gauge, 1.5-inch needle is typically used for delivery.

Due to the liposomal nature of the local analgesic, it is important to inject the solution while simultaneously withdrawing the needle through the soft tissue. The liposome solution will not disperse through the tissue on its own. It must be placed in a deliberate nature around the arthroto-my and posterior capsule for effective analgesia.

The use of bupivacaine liposome injectable solutions provides an analgesic alternative in TKA procedures, which can lead to patients participating in physical therapy sooner and reduce the risk of developing joint stiffness. This reduces the need for subsequent procedures and promotes the best possible functional outcomes for patients. While research is still being conducted to determine the impact of its use, there seems to be positive results thus far.
ABOUT THE AUTHOR
Paul Halfman, CST, works on the orthopedic surgical team for Northwestern Medicine at Central DuPage Hospital in Winfield, Illinois. He is a chairperson on the Perioperative Services Shared Governance Committee for Best Practice and serves as a member of the Interview Council for Perioperative Services. He received a Bachelor’s of Science from Loyola University of Chicago in Chemistry and an associate degree from Robert Morris University in surgical technology where he trained at The University of Chicago Medical Center.

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1. The femoral nerve originates at the second, third and _______ lumbar nerve.
   a. Fifth
   b. First
   c. Fourth
   d. Eighth

2. Analgesic alternatives to the single shot femoral nerve block include techniques such as:
   a. Continuous infusion femoral nerve catheter
   b. Injection of bupivacaine hydrochloride
   c. Injection of non-bupivacaine based local anesthetic
   d. None of the above

3. Engineered _______ can be constructed to contain items such as drugs or genetic material in the lumen or within layers of its shell.
   a. Bubbles
   b. Liposomes
   c. Membranes
   d. Injections

4. A total knee arthroplasty is typically performed to correct osteoarthritis of the articular surfaces of the _______.
   a. Femur
   b. Tibia
   c. Patella
   d. All of the above

5. The liposome solution is injected directly into the surgical wound at which point of the procedure?
   a. At the beginning
   b. After 15 minutes
   c. At closing
   d. Halfway

6. The main benefit of the liposomal delivery system is that a single intraoperative injection can have an analgesic effect for as long as _______ as the membrane is metabolized.
   a. 56 hours
   b. 60 hours
   c. 72 hours
   d. 80 hours

7. After a spinal block has been administered, the patient is placed in the _______ position.
   a. Supine
   b. Prone
   c. Trendelenburg
   d. Lateral

8. According to the article, which bone usually receives the first trial implant?
   a. Patella
   b. Tibia
   c. Femur
   d. Fibula

9. Patient benefits of using of bupivacaine liposome injectable solutions includes _______.
   a. Reducing the need for subsequent procedures
   b. Allows for physical therapy sooner post-op
   c. Reduces the risk of developing joint stiffness
   d. All of the above

10. The liposome injection solution should be injected into the _______ portion of the joint capsule.
    a. Parietal
    b. Medial
    c. Posterior
    d. Distal

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