ISSN: 1607-8322, e-ISSN: 2220-5799 **Anaesthesia, Pain & Intensive Care**
Vol 27(6); December 2023 DOI:10.35975/apic.v27i6.2356

ORIGINAL RESEARCH **REGIONAL ANESTHESIA**

The incidence of post amputation syndrome after pericapsular nerve group block versus sciatico-femoral nerve block in patients undergoing above knee amputation

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ABSTRACT

Background & objective: Regional anesthesia for orthopedic procedures has been widely practiced around the globe, and it has been employed either alone or in combination with general anesthesia. An above knee amputation will need blockade of both femoral and sciatic nerves for successful pain control and help with peripheral sensitization for the patient. Pericapsular nerve group (PENG) block is a novel regional nerve block to provide analgesia in fractured hip patients. We assessed the effectiveness of this block compared to sciatico-femoral block and the incidence of post amputation syndrome in patients undergoing above knee amputation.

Methodology: This randomized controlled single-blinded study was carried out on 30 patients with lower limb bone tumors indicated for above knee amputation admitted to surgery clinic, National Cancer Institute, Cairo University. The duration of study was from January 2021 to May 2022. Patients were randomized equally using opaque sealed envelopes into 2 groups Group A: (n = 15) pericapsular nerve group block group (PNGB) to receive 20 mL of 0.125% bupivacaine with 4 mg dexamethasone at the pubic ramus just medial to the anterior inferior iliac spine (AIIS). Group B: (n = 15) patients received sciatico-femoral block with a mixture of 20 mL 0.125% bupivacaine with 4 mg dexamethasone injected in the femoral and sciatic nerve. Postoperative VAS scores, the time to first analgesic request was and the total morphine consumed as rescue analgesic were recorded.

Results: Time to first analgesic request was significantly prolonged in group B than group A ($P < 0.001$). Total morphine dose in first 24 h postoperative and in first 48 h postoperative were significantly lower in group B than in group A ($P < 0.001$ and 0.003 respectively). VAS scores were significantly lower at 2, 4 and 8 h in group B than group A ($P < 0.05$) and were insignificantly different at 12, 24 h, and on 2nd and 7th day between the two groups. Phantom limb syndrome frequency was significantly lower at 1, 2, 3 and 6 months in group B than in group A ($P < 0.05$); at 6 mo it was noted in 10 (66.67%) patients in group A and 4 (26.67%) in group B with 2.5 (1:6.23) RR (95% CI) ($P = 0.028$).

Conclusions: Sciatico-femoral block has better outcomes than pericapsular nerve block in patients undergoing above knee amputation regarding analgesic effect and the development of phantom limb syndrome.

Abbreviations: AIIS - Anterior Inferior Iliac Spine; PNGB - Pericapsular Nerve Group Block; PLP - Phantom Limb Pain; SFB - Sciatic–Femoral Nerve Block; VAS – Visual Analog Scale

Key words: Above Knee Amputation; Peri Capsular Nerve Group Block; Post Amputation Syndrome; Sciatico-femoral Nerve Block

Citation: Bakeer AHMH, Hussien AIH, Abd El Aziz El Shaikh SM, Soliman Idris AM. The incidence of post amputation syndrome after pericapsular nerve group block versus sciatico-femoral nerve block in patients undergoing above knee amputation. Anaesth. pain intensive care 2022;27(2):665−672; **DOI:** 10.35975/apic.v27i2.2356

Received: May 11, 2023; **Revised:** September 08, 2023; **Accepted:** September 17, 2023

1. INTRODUCTION

Looking at data from the Amputee Coalition, every year 185,000 amputations are being carried out in the United States. This means that on an average, two million people have been living with an amputated extremity in the United States alone.[1] Other data to consider is just as alarming; globally, there are 1 million amputations annually. This is an estimated 1–2 amputation per minute. Lower limb amputations are the most common, with most being due to vascular disease. 85% of lower limb amputations are preceded by a foot ulcer. About half of the people with diabetes who get a lower limb amputation will receive a second amputation.[2] African American populations are four times more likely to get an amputation than Caucasian.[3] Around a third of these patients have persistent depression and anxiety after the amputation.[4]

The loss of a body part can lead to pain and other sensations that fall into three distinct descriptive categories, namely phantom sensations, phantom pain, and residual pain. Phantom sensations are defined as pain-free perceptions emanating from the lost body part after deafferentation, and phantom pain is a painful or unpleasant sensation in the distribution of the lost or deafferented body part.[5] Phantom sensations can be a different expression of phantom pain and interfere with rehabilitation therapy by enhancing and interacting with phantom pain.[6]

Phantom limb pain (PLP) can occur in up to 85% of patients after a limb amputation.[7] but is common in the first six months after surgery.[8] Although many previous studies have reported risk factors for PLP, such as pre-amputation pain, cause of amputation, prosthesis use, and peri-operative analgesia, the exact causes remain unknown.[9] Unanswered questions still surround the underlying mechanisms of PLP, there seems to be a solid theoretical basis for the role of peripheral mechanisms as well as central neural mechanisms.[10]

The current standard of care is pre-operative nerve blockade to prevent peripheral sensitization leading to future onset of phantom limb pain. A consultation with the Acute Pain Service or similar entity that performs peripheral nerve blockade pre-operatively and then follows the patient during their post-operative inpatient course is an important factor in the success in early prevention of acute and chronic pain for these patients.

Most patients that arrive for amputations should be evaluated to receive pre-operative peripheral nerve blocks. If this cannot be done pre-operatively, patients can be evaluated post-operatively for a nerve block. If patients do not require post-operative anti-coagulation that will preclude a continuous peripheral nerve catheter, this would be the preferred nerve block for these patients as this will help with prevention phantom limb pain and chronic post-operative pain.[11,12] This can be utilized for 3–5 days. An above the knee amputation will need blockade of both femoral and sciatic nerves for successful pain control and help with peripheral sensitization for the patient.[13]

There is no comparison of epidural to peripheral nerve catheters for lower extremity amputations, but on a practical note, peripheral nerve blockade will allow better mobilization and participation in physical therapy.[11] In addition, peripheral nerve block does not have the hemodynamic affects that epidural blockade can have.[11]

Pericapsular nerve group block or PENG block is a novel regional nerve block to provide analgesia in fractured hip patients.[14,15] It is primarily an ultrasound-guided (USG) technique where target area is the pelvic rim (superior pubic ramus) near iliopectineal eminence, deep to fascia of iliopsoas muscle.[14] Articular branches of femoral nerve and accessory obturator nerves, which cross over the bony rim, are primary targets of the PENG block.[14] However, by increasing volume of local anesthetic drug, other nerves (obturator, femoral, genitofemoral, and lateral femoral cutaneous nerve) can be blocked.[16] The indications of this block are increasing.[17] Other than its perioperative use and analgesia for hip surgeries, PENG block has been used for surgical anesthesia to reduce the dislocated hip and varicose vein striping procedure.[18,19]

PENG block, which also is a plane block, was described recently by Girón-Arango et al. for postoperative analgesia in orthopedic surgery.[14] This block is a new regional anesthesia technique based on blocking the femoral nerve (FN) and accessory obturator nerve (ON) with a single injection.[18,20]

We compared the effectiveness of peri-capsular nerve group block and sciatico-femoral nerve block in the post amputation syndrome in patients undergoing above knee amputation.

2. METHODOLOGY

This randomized controlled trial was carried out on 30 patients with lower limb bone tumors indicated for above knee amputation admitted to surgery clinic, National Cancer Institute, Cairo University, from January 2021 to May 2022 after approval by the Ethics Committee of Faculty of Medicine, Cairo University, Egypt. An informed written consent was obtained from each patient. All data of patients were confidential with secret codes and private file for each patient, all data were used for the current medical research only. Any unexpected risks appearing during the course of the research were explained to the participants and the ethical committee on time.

Inclusion criteria were; ASA class I and II, 20 to 60 y of age, undergoing above knee amputation due to any type of cancer. Exclusion criteria were patient refusal, local infection at the puncture site, coagulopathy, cognitive disorders, unstable cardiovascular disease, history of psychiatric disorders or drug abuse or allergies to medication used.

Patients were randomized using opaque sealed envelopes into two equal groups; Group A: (n = 15) pericapsular nerve group block group (PNGB) to receive 20 mL of 0.125% bupivacaine with 4 mg dexamethasone administered at the pubic ramus just medial to the anterior inferior iliac spine (AIIS). Group B: (n = 15) patients received sciatico-femoral block received 20 mL of 0.125% bupivacaine with 4 mg dexamethasone injected in the femoral and sciatic nerve under US guidance.

Upon arrival in the operating room, electrocardiography, pulse oximetry, and noninvasive blood pressure monitoring was instituted, All patients underwent above knee amputation under general anesthesia. The blocks were performed after the end of surgery and before the recovery of the patients by the same investigator using the ultrasound machine (Philips CX50 Extreme edition) equipped with high frequency probe.

2.1. Group A: PNGB group

Under aseptic precautions, the block was administered under ultrasound guidance with low frequency curvilinear probe. The probe was placed parallel to the inguinal crease, at the level of anterior superior iliac spine. The scanning was done with gradual caudad movement of the probe. After AIIS become visible, the probe was turned slightly medial until the hyperechoic continuous shadow of superior pubic ramus become visible. The psoas muscle with prominent tendon was identified just above the pubic ramus. The target was the plane between these two structures. Aligning the pubic ramus in the center of the image and targeting the pubic ramus just medial to the AIIS, a standard 25G Quincke needle was introduced and 20 mL 0.125% bupivacaine with 4 mg dexamethasone was administered using ultrasound-guided out-of-plane technique.

2.2. Group B: Sciatico-Femoral Block Group

After draping the inguinal region, the femoral nerve was identified lateral to the femoral artery using a 5-13 MHz linear phased array transducer. Under ultrasound guidance, a 25G Quincke needle was introduced toward the femoral nerve parallel to the ultrasound beam, and 20 mL of 0.125% bupivacaine with 4 mg dexamethasone was injected near the femoral nerve. The trajectory of the needle was adjusted to achieve even distribution of the local anesthetics around the femoral nerve. Then, the patient was placed in the lateral position with the hip and knee joints flexed by 30° to 50°. Following the identification of the sciatic nerve located in the intermuscular plane of the gluteus maximus and gluteus medius muscles between the ipsilateral ischial tuberosity and greater

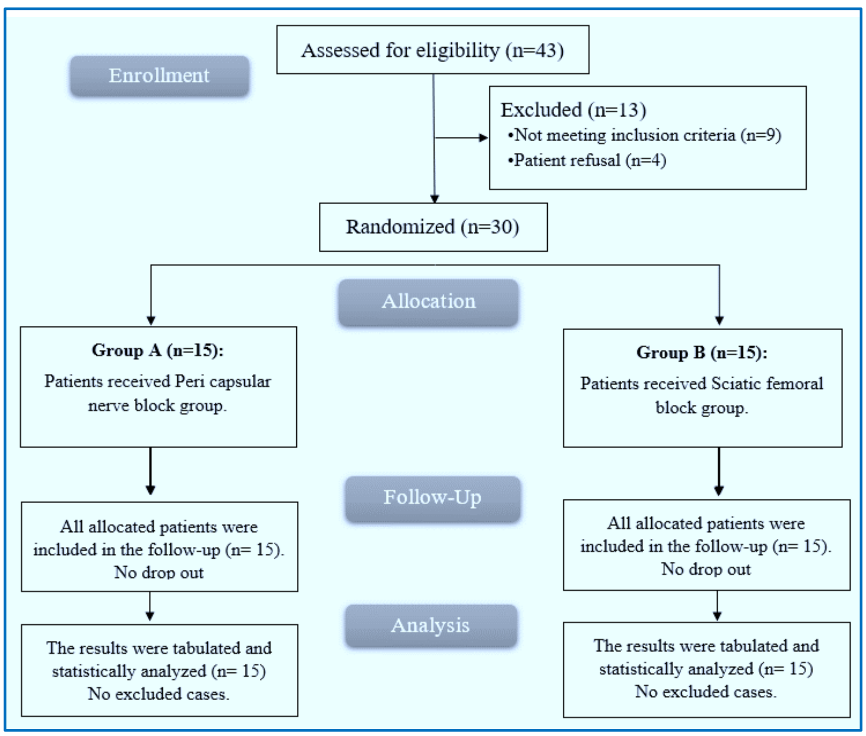

Figure 1: Consort flow diagram of the participants through each stage of the trial

trochanter using a convex phased array transducer, 20 mL of 0.125% bupivacaine with 4 mg dexamethasone was

placed near the sciatic nerve through the 22G Tuohy needle. The needle was introduced from the lateral side using the in-plane technique.

Demographic data including age, sex and weight, hemodynamic data (mean arterial blood pressure, heart rate, oxygen saturation, respiratory rate) were recorded at admission, 30 min post block and 6 h post block. PaO2 / FiO2 ratio was noted at admission, 30 min post block and 6 h post block.

Table 1: Patient characteristics of the studied groups

Parameters		Group A (n = 15)	Group B (n = 15)	P value
Age (y)	Mean ± SD	35.53 ± 10.84	43.53 ± 12.63	0.073
	Range	21-58	23-60	
Sex [n (%)]	Male	10 (66.67%)	11 (73.33%)	0.690
	Female	5 (33.33%)	4 (26.67%)	
Weight (kg)	Mean ± SD	74.33 ± 7.03	71.8 ± 5.92	0.295
	Range	62-84	60-82	
Height (m)	Mean ± SD	1.66 ± 0.07	1.61 ± 0.06	0.061
	Range	1.52-1.77	1.53-1.73	
BMI (kg/m^2)	Mean ± SD	27.14 ± 3.54	27.76 ± 3	0.609
	Range	21.4-34.6	22.5-32	
ASA	ASA II	15 (100%)	15 (100%)	---

BMI: Body mass index, ASA: American Society of Anesthesiologists.

Data presented as Mean **±** *SD, or n (%) or n.*

Any adverse effects were recorded including hypotension (mean arterial blood pressure less than 60 mmHg), signs of local anesthetic toxicity or respiratory depression.

Length of ICU stay (days) as well as the length of hospital stay (days) by the patients were also recorded.

2.3. Outcome measures

The primary outcome was the assessment of the efficacy of PENG block in reducing the post amputation limb pain for 24h and to compare it with the efficacy of sciatico-femoral nerve block in reducing the post amputation limb pain as well. The secondary outcome was the assessment of the efficacy of PENG block in reducing the phantom limb syndrome during the first 6 months post operatively and to compare it with the efficacy of sciatico-femoral nerve block. Also to assess and compare the efficacy of both blocks in reducing the post-operative needs of rescue narcotics.

2.4. Sample size

Based on a study by Shankar et al. (2020), who found that mean VAS score 24 h post-operative in PENG block was 6.3 ± 0.8. In Cook et al. (2003) the mean VAS score 24 h post-operative in those who received sciatico-femoral block was 4.4 ± 2.1.

A sample size of 26 (13 per group) was sufficient to detect a power of 80% and a significance level of 5%.

The number was increased to a total sample size of 30 (15 per group) to allow for the use non-parametric test.

Sample size estimation was performed by G power statistical package.

2.5. Statistical analysis

Data analyses was analyzed using IBM SPSS Statistics Version 22. Quantitative data was presented as mean ± standard deviation or median and ranges as appropriate. Qualitative data was presented as numbers and percentages. Numeric data was explored for normality using Kolmogrov-Smirnov test and Shapiro-Wilk test. Comparisons between the two groups for normally distributed numeric variables was done using the Student's t test, and for non-normally distributed numeric variables, comparisons between two groups was done by Mann-Whitney test. Comparing categorical variables was done by using chi-square test or fissure exact test as appropriate. P was significant at 0.05 levels. All tests were two tailed.

3. RESULTS

In this study, 43 patients were assessed for eligibility, 9 patients did not meet the criteria and 4 patients refused to participate in the study. The remaining patients were randomly allocated into two equal groups (15 patients in each). All allocated patients were followed-up and analyzed statistically (**Error! Reference source not found.** 1).

Patient characteristics were insignificantly different between both groups (Table 1).

The mean time to first analgesic request was significantly less in group A compared to group B ($P < 0.001$). The mean total morphine dose in first 24 h as well as in first 48 h postoperative was significantly more in group A than in group B (P < 0.001 and 0.003 respectively) (Table 2).

Table 2: Comparative postoperative pain relief

Parameter	Group A (n = 15)	Group B (n = 15)	P value
Time to first analgesic request (h)	3 ± 0.93 (2-5)	7.07 ± 1.1 (5-8)	< 0.001*
Total morphine dose in first 24 h (mg)	13 ± 3.68 (10-20)	8.67 ± 2.29 (5-10)	< 0.001*
Total morphine dose in first 48 h (mg)	18.33 ± 3.09 (15-25)	14.33 ± 3.72 (10-20)	0.003*

** Significant as P ≤ 0.05; Data presented as mean ± SD (range)*

Table 2: Comparative VAS scores of postoperative pain

Time to measure	Group A (n = 15)	Group B (n = 15)	P value
2 h	1 (0.5-4)	1 (0-1)	< 0.001*
4 h	2 (1-2)	1 (0.5-1.5)	< 0.001*
8 h	4 (2.5-5.5)	1 (1-4)	0.045*
12 h	3 (2-4)	3 (2.5-4.5)	0.468
24 h	3 (2-4.5)	3 (2-4.5)	0.866
2nd day	4 (2-4.5)	4 (2-4.5)	0.658
7th day	3 (2-6)	4 (2.5-5)	0.487

** Significant as P ≤ 0.05, VAS: Visual Analog Scale.*
Data presented as mean (range)

Table 3: Comparative VAS of phantom limb syndrome over 6 months

Period	Group A (n = 15)	Group B (n = 15)	P value
1 mo	5 (2-6.5)	2 (1-3.5)	0.037*
2 mo	4 (1.5-6)	2 (0.5-3.5)	0.046*
3 mo	4 (2-6)	2 (1-3.5)	0.037*
6 mo	3 (3-5.5)	3 (2-3.5)	0.016*

** Significant as P ≤ 0.05, VAS: Visual Analog Scale.*
Data presented as mean (range)

VAS measurements were significantly lower at 2, 4 and 8 h in group B than group A (P < 0.05) and were insignificantly different at 12, 24 h, and at 2nd day and 7th day between two groups (**Error! Reference source not found.**).

VAS scores for phantom limb syndrome measurements were significantly lower at 1, 2, 3 and 6 mo in group B than group A (P < 0.05)(**Error! Reference source not found.**).

The incidence of phantom limb syndrome at 6 m was 10 (66.67%) in group A and 4 (26.67%) in group B with 2.5 (1:6.23) RR (95% CI). Incidence of phantom limb syndrome was significantly lower in group B than in group A (P = 0.028).

4. DISCUSSION

Patients who have an above knee amputation (AKA), a non-traumatic major lower limb amputation (MLEA), frequently have numerous comorbidities like diabetes mellitus, cardiovascular and renal disorders, and they are at risk for postoperative morbidity and mortality.[21]

After limb salvage therapy has failed, AKA is the last option. It is used in overwhelming soft-tissue or bone infections as an emergency measure to quickly contain the infection source. According to one research, ASA grade 4 patients undergoing MLEA had 30-day mortality that was more than four times higher, and long-term mortality that was twice as high. The prognosis for those who endure AKA, is grim.[22]

An innovative method used with ultrasound guidance is the PENG block. Girón-Arango and colleagues characterized it in 2018 as blocking the articular branches of the femoral nerve, obturator nerve, and accessory obturator nerve. It has been used effectively as a regional anesthesia technique to control hip surgery pain without impairing motor function. The efficacy of

PENG block in reducing hip fracture pain has been the subject of numerous studies; however, additional research is needed to fully understand its function.[23-25]

Since the patients are frequently very sick, general anesthesia can be risky. Instead of using a general anesthetic, neuraxial (spinal or epidural) anesthesia is frequently used, but even this approach has its drawbacks because spinal or epidural anesthesia can cause blood pressure to fall in patients who already have compromised cardiovascular systems or are sick. An alternative method involves performing a regional sciatic nerve block in conjunction with a femoral nerve block, a 3-in-1 block, or a psoas compartment lumbar plexus block. When the two blocks are combined, relatively large doses of local anesthetic agents will be used, so it's important to keep in mind the utmost safe dose of the agent.[26]

Our study showed that time to first analgesic request was significantly prolonged in group B than group A ($P < 0.001$). Total morphine dose in first 24 h postoperative and total morphine dose in first 48h postoperative were significantly lower in group B than group A ($P < 0.001$ and 0.003 respectively).

VAS measurements were significantly lower in group B than in group A ($P < 0.05$), but the difference was insignificant after 12 h.

VAS of phantom limb syndrome measurements was significantly lower at 1mo 2 nad later on in group B than group A ($P < 0.05$). The incidence of phantom limb syndrome was significantly lower in group B than group A ($P = 0.028$).

Shamim et al. (2018)[27] carried out a case series reporting five patients for urgent or emergent lower limb amputations that were successfully carried out under ultrasound-guided sciatico-femoral nerve blocks. Only one patient with AKA complained of moderate pain on medial side of thigh, for which lignocaine 1% was infiltrated at incision site. All patients were successfully managed with peripheral nerve blocks, and they remained hemodynamically stable and pain-free postoperatively.

Baddoo et al. (2009)[26] published a case series of 10 AKA cases in which they used landmark technique of "three in one femoral nerve block" and Labat's approach of sciatic nerve block. Some patients were given a sciatic block combined with three-in-one block and the remainder were given a sciatic nerve block combined with a psoas compartment lumbar plexus block. The only patient undergoing below knee amputation was given a sciatic nerve block (SNB) combined with a femoral nerve block. The decision on whether to use the anterior or posterior approach for the sciatic nerve block and whether to use a 3-in-1 block or lumbar plexus block (LPB) depended mainly on whether the patient could easily be turned onto their side (the posterior approach for a SNB and a LPB will need the patient on their side). The time interval between the end of surgery and the time the first dose of analgesic needed ranged between 5-30 h with a mean of 12.5 h. However, they encountered partial block failure in three cases. One reason for this was the lack of ultrasound, which has transformed the current regional anesthesia practice.

Chandran et al. (2018)[21] carried out a similar study to evaluate the use of peripheral nerve blocks as the sole anesthetic technique in the AKA population and its clinical outcomes. Sixty-seven percent received combined femoral, obturator and sciatic (FOS) nerve blocks, in which nine cases had an additional lateral femoral cutaneous nerve (LFCN) block (lateral FOS). The rest of the patients had combined femoral and sciatic nerve (FS) blocks. The FS group required higher sedation and analgesia compared to the FOS and FOSL groups ($P = 0.013$). Most of the patients were hemodynamically stable during operation except for 10 patients which required a vasopressor during operation. Patients in our study had a 1-year survival of 53%. The 30-day mortality was noted as 12%. The intraoperative mortality within 48 h after surgery was observed to be zero. The earliest recorded death was on the sixth postoperative day.

Hussein et al. (2020)[28] conducted a study to compare unilateral spinal anesthesia and ultrasound-guided combined sciatic–femoral nerve block (SFB) regarding hemodynamic stability, quality of nerve block, bladder function, and time-to-readiness for discharge (TRD) in below-knee amputation surgery. A total of 80 patients who underwent knee amputation surgery were enrolled in the study. They were randomly assigned to one of two groups; Group A received 2 ml (10 mg) of 0.5% levobupivacaine, and group B (SFB) received 25 ml containing 10 ml of 2.0% lidocaine, 10 ml of 0.5% levobupivacaine and 5 ml of saline (15 ml of femoral and 10 ml of sciatic nerve block). Onset of sensory and motor blocks was significantly shorter in group A, whereas the recovery time for sensory and motor blocks was longer in group B compared with group A. There was a decrease in time for spontaneous urination, increase in time for first analgesic need, and decrease in time to early discharge in group B as compared with group A, which was statistically significant. The pain score was significantly lower in group B after surgery. Satisfaction of patients was significantly higher in group B compared to group A.[28]

Regarding sciatic dosing, the choice of local anesthetic and dose administered is dependent on the type of surgery. For example, for knee arthroplasty, a low concentration of 20 ml ropivacaine (0.16%) is all that is required to block the sciatic nerve for 12 to 16 h. On the other hand, for relieving the pain of amputation surgery, choice of local anesthetic does not matter as sensory-motor separation is not an issue. Nevertheless, the concentration of local anesthetic both as a bolus and within an infusion should be sufficiently high to provide long-lasting pain relief. Typically, a bolus of 0.375–0.5% followed by an infusion of 0.2–0.25% levobupivacaine or a ropivacaine 0.2% infusion at 5 ml/h with patient-controlled bolus 5ml/h will provide good analgesia. Sciatic nerve block provides postoperative pain relief after below knee amputation, knee replacement, foot, and ankle surgery.[29]

Regarding femoral block, the practice is to administer a 20 ml bolus of ropivacaine (0.16%), prepared with a four-fifth dilution of commercial 0.2% ropivacaine using sterile saline. The advantage of such a low concentration is to provide profound analgesia while allowing straight leg raising in the immediate postoperative period, facilitating enhanced recovery with excellent pain relief. No substantive evidence exists regarding the relative potency of ropivacaine and levobupivacaine using single-shot femoral block for postoperative pain relief. Levobupivacaine 0.16% is equally efficacious but more likely to be associated with a limitation of straight leg raising in some patients.[30]

The perineural infusion is commenced 7–8 h after the femoral bolus, to allow confirmation of spinal regression, assessment of pain, examination of knee flexion and extension, and straight leg raising. Nursing staff can then be encouraged to mobilize the patient once straight leg raising is established. At this time, a well-conducted femoral block using 0.16% ropivacaine is associated with pain relief on movement consistent with a VAS score between 15 and 30 mm. Breakthrough pain is generally indicative of a poor block.[30]

Persistent pain following surgery can have neuropathic characteristics, and many of the surgeries associated with persistent pain, such as thoracotomy, breast surgery and amputation, involve major nerves in the surgical field.[31]

Effective regional anesthesia may prevent central sensitization by blocking nociceptive input into the spinal cord. Epidural anesthesia and paravertebral blocks reduce the risk of persistent pain after open thoracotomy and breast cancer surgery, respectively.[32] These findings are interesting also in view of the apparent beneficial effect of regional anesthesia in reducing tumor recurrence.[33] Regional anesthesia has been advocated in oncological surgery to reduce the risk of cancer recurrence, based on some evidence by the inhibition of tumor cell seeding and growth by various pathways. These include effective suppression of the adrenergic and inflammatory response to surgery, preservation of immune function and direct action of systemic local anesthetics on tumor cell apoptosis, and indirectly through reduction in the use of opioids which may have their own pro-metastatic effects.[33]

5. LIMITATIONS

It was a single-center study, and the results may differ elsewhere. Sample size was small. There was no assessment of hemodynamics.

6. CONCLUSION

Sciatica femoral block has better outcomes than pericapsular nerve block in patients undergoing above knee amputation regarding postoperative pain relief and phantom limb syndrome.

7. Data availability

The numerical data generated during this research is available with the authors.

8. Ethical issues

The study was approved by the Ethics Committee of Faculty of Medicine, Cairo University, Egypt. An informed written consent was obtained from each patient.

9. Conflict of interest

Authors declare no conflict of interests. The study utilized departmental resources, and no external or industry funding was involved.

10. Authors' contribution

AB: Corresponding author

AH, AS: Concept, conduct of the study

SS: Literature search

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