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Effect of Nalbuphine as Adjuvant to Bupivacaine for Ultrasound-Guided Popliteal Nerve Block: A Prospective Randomised Comparative Clinical Study

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Abstract

Introduction: Popliteal nerve block is a useful technique for ankle and foot surgeries as it avoids complications in elderly who are prone for hemodynamic changes leading to increased morbidity and mortality. There is advantage of early post operative mobility which is essential in orthopaedic surgeries and absence of post dural puncture headache. Nalbuphine is a derivative of 14-hydroxymorphine which is a strong analgesic with mixed k agonist and μ antagonist action.The primary aim of study is to evaluate effect of adding Nalbuphine to Bupivacaine in popliteal nerve block in terms of onset and duration of sensory and motor blockade and duration of analgesia. *Study Design:* A prospective randomised comparative clinical study. *Materials and Methods:* After obtaining institutional ethical committee clearance. Sixty patients between 18 -70 years of either sex with ASA status I, II, III posted for ankle and foot surgeries were grouped randomly into two groups using simple sealed envelope method with 30 in each group. After getting informed consent from patients detailed pre anaesthetic evaluation was done on previous day of surgery. Group A received 20ml of Bupivacaine with 1ml of normal saline and group BN received 20ml of Bupivacaine with 1ml of 10mg Nalbuphine. Data presented as mean and standard deviation. The t-test was used to examine the differences between means. Statistical significance was accepted for a $p < 0.05$. *Results: Sensory blockade:* In our study we found that Group BN patients who received Nalbuphine as additive provided faster onset of sensory level blockage with mean time of onset value being 11.8 ± 2.4 (in mins) compared to Group A where mean value was 15.20 ± 1.80 (in mins) . The results were statistically significant with a p value of <0.001**. The duration of sensory level block in Group BN who received Nalbuphine as additive was 760 ± 23.3 compared to Group A where mean value was 552 ± 19 with statistically significant p value of <0.001**. *Motor blockade:* In our study we found that Group BN patients who received Nalbuphine as additive provided faster onset of motor level blockage with mean time of onset value being 14.7 ± 1.5 (in mins) compared to Group A where mean value was17.6 ± 1.1(in mins) . The results were statistically significant with a p value of <0.001**. The duration of motor level block in Group BN was 573 ± 20.6 compared to Group A where mean value was 438 ± 18.4 with statistically significant p value of <0.001**. *Conclusion:* This study demonstrates that addition of 10 mg nalbuphine to bupivacaine in popliteal nerve block in patients undergoing ankle and foot surgeries decreases time of onset of anaesthesia, shows significant increase in duration of sensory and motor blockade and also increases the post operative analgesia.

Keywords: Popliteal nerve block; USG guided; Bupivacaine nalbuphine.

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Introduction

Regional anaesthesia techniques are used frequently as an alternative to general anaesthesia in ambulatory orthopaedic and surgical procedures For ankle and foot surgeries, particularly in patients thought unsuitable for central neuraxial block popliteal nerve block is a reliable technique. It avoids complications in elderly patients who are particularly prone for hemodynamic changes leading to increased morbidity and mortality[1]. It is associated with advantage of early post operative mobility which is essential in orthopaedic surgeries. Another advantage of popliteal nerve block over central neuraxial block is its avoidance of post dural puncture headache, making it an ideal technique for ambulatory surgeries. It can be used more readily in the presence of minor degree of coagulopathy or after head injury where central neuraxial block is relatively contraindicated[1].

Long acting local anaesthetics (LA) are commonly used for popliteal nerve block as they provide prolonged post operative analgesia and bupivacaine is the most commonly used LA for this purpose. The analgesic duration after peripheral nerve blockade with bupivacaine is longer than[2] or the sameas the duration of analgesia provided by ropivacaine.[3] Furthermore, bupivacaine is less expensive compared to levobupivacaine or ropivacaine.

Nalbuphine is a derivative of 14-hydroxymorphine which is a strong analgesic with mixed k (kappa) agonist and μ(mu) antagonist action with its analgesic effect been found to be equal to that of morphine but unlike it has a ceiling effect on respiration. Nalbuphine has the potential to maintain or even enhance μ-opioid based analgesic effect while simultaneously mitigating the μ-opioid side effects.[4]

The primary aim of this study is to evaluate the effect of adding Nalbuphine to Bupivacaine in popliteal nerve block in terms of onset of sensory and motor blockade, duration of sensory and motor blockade and duration of analgesia.

Materials and Methods

The study was a hospital based prospective, randomised , comparative clinical study. The study population consisted of 60 patients aged between 18-70 years of either sex with ASA physical status I, II and III, posted for elective ankle and foot surgeries who met the predefined inclusion and exclusion criteria. The study was conducted from April 2017 to January 2019 in RajaRajeswari Medical College and Hospital, Kambipura Bangalore after obtaining a clearance from the institutions ethical clearance committee and a written informed consent from all the patients included in the study. The patients were randomly divided into two groups using simple sealed opaque envelope method with 30 patients in each group (n = 30). Group A received 20ml of Bupivacaine with 1ml of normal saline and Group BN received 20ml of Bupivacaine with 1ml of 10mg Nalbuphine.

Selection of Patients

Inclusion Criteria

1. ASA physical status I, II and III of either sex
2. Aged between 18-70 years
3. Admitted for Ankle and Foot surgeries.

Exclusion Criteria

1. Patients with known hypersensitivity or contraindications to the study drugs
2. Infection at the site of block
3. Patients with advanced renal, hepatic, respiratory or cardiac diseases
4. Patients with severe coagulopathy
5. Pregnant patients
6. Patients with neurological, psychiatric or neurovascular disorders
7. Patient with alcohol/drug abuse
8. Patient refusal

Methodology of Study

After obtaining institutional ethical committee clearance, 60 adult patients aged be- tween 18-70 years of either sex with ASA physical status II and III, posted for ankle and foot surgeries were grouped randomly into two groups using simple sealed envelope method with 30 patients in each group. (n = 30). An informed consent was obtained from all patients and detailed pre anaesthetic evaluation was done on the previous day of surgery.

All patients were nil per orally for 6 hours for solids and 2 hours for liquids prior to surgery. Tab Alprazolam 0.25mg and Tab Ranitidine 150 mg was given on the previous night of surgery. Anaesthesia machine was checked and all the drugs and equipments necessary for emergency resuscitation was kept ready. On receiving the patient in operating room, a wide bore intravenous line was secured with 18 gauge (G) cannula.

Monitoring for electrocardiography (ECG), heart rate (HR), arterial pulse saturation (SpO_2) and non invasive blood pressure (NIBP) was done for all patients.

The sciatic nerve is considered a nerve bundle with two separate nerves: tibial and common peroneal. These two components eventually diverge 5–10 cm proximal to the crease of the popliteal fossa. The injection of local anaesthetic must occur within the sciatic nerve sheath that contains both components of the nerve. The injection is ideally accomplished at the position where both components of the nerve are within the sheath but slightly separated by adipose tissue, allowing for safe placement of the needle between them[6]. The patient was placed in the lateral position and beginning with the transducer in the transverse position at the popliteal crease, the popliteal artery was identified, aided with colour Doppler US when necessary, at a depth of approximately 3–4 cm. Just superficial to the popliteal artery the popliteal vein accompanies it. The biceps femoris muscles and the semimembranosus and semitendinosus muscles are visualised on either side of the artery. A hyperechoic, oval structure with a honeycomb pattern is seen superficial and lateral to the vein which is the tibial nerve[6,7].

To visualise the tibial and peroneal nerves the transducer should be slid proximally as they come together to form the sciatic nerve before its division. This junction usually occurs at a distance 5–10 cm from the popliteal crease but may vary in different patients. After negative aspiration for blood, test solution (20ml of 0.5% bupivacaine with either 1ml Normal Saline or 1ml 10mg Nalbuphine) was injected. Time of completion of injection was taken as time zero. Test drug was prepared and loaded in two 10ml syringes with one syringe having either 1ml Normal Saline or 1ml 10mg Nalbuphine by an anaesthesiologist who is not involved in the study. All the blocks were performed by the same investigator.

Immediately following popliteal nerve block patients were placed in supine position. Sensory block was assessed by pin prick test using 27G blunt needle every 5 minutes for the onset of block on the dorsal and plantar aspects of the foot and sensation was categorised as[8];

0 = sharp (normal sensation as of contra lateral limb)

1= dull (pin prick perceived as pressure)
2 = absent (complete loss of awareness of pinprick)

Motor block was assessed every 5 minutes for the onset by assessing plantar or dorsiflexion at the ankle and was graded as[8];

0 = normal power

1 = reduced power

2 = complete motor block

Onset of sensory and motor block, duration of blocks, quality of block were observed and noted.

Patients were assessed for hemodynamic parameters every 5 minutes till the complete onset and also at the end of surgery . Patients were monitored for any signs and symptoms of cardiovascular (changes in heart rate, rhythm) and central nervous system toxicity. They were also monitored for signs of hypersensitivity reactions to local anaesthetic drugs. Patient satisfaction with the anaesthetic technique was recorded by asking the patient and surgeon to assess the block as : very good, good, medium or poor. In the post operative period, the pain was assessed by Visual Analogue Score and at a score of >4, patients were given analgesics like inj. Tramadol 50mg or inj. Diclofenac 75mg and the study concluded at this point.

Authors do not have financial gain from any of the products used and the study is not sponsored by any company.

Sample Size of Estimation

Data was collected and entered in MS Excel and analysed using SPSS version 2.0. Descriptive statistics includes frequencies, percentage and mean standard deviation. Student t-test will be used to test the significant differences between the two groups. The sample size is calculated using the following formula[9]:

$n = 2 (Z_{\alpha} + Z_{1-\beta})^2 * \sigma^2, \Delta^2$

where ‗n' is the required sample size.

For Z_{α}, Z is a constant (set by convention according to the accepted α error)

α-error =5%, therefore Z_{α} is 1.96

For $Z_{1-\beta}$, Z is a constant (set by convention according to power of the study)

Power of the study is 80%, therefore $Z_{1-\beta}$ is 0.8416

σ is the standard deviation (estimated) which is 0.55

Δ the difference in effect of two interventions which is required (estimated effect size),

Which is 0.4 in our study, keeping in mind the difference in effect of two interventions are 40%.

By applying the formula,

$n = 2 (Z_{\alpha} + Z_{1-\beta})^2 * \sigma^2, \Delta^2$

$n = 2 (1.96 + 0.8416)^2 * (0.55)^2 (0.4)^2$

Therefore, n = 29.6

29.6 patients will be required in each group according to the calculation. Therefore, we will be recruiting 30 patients in each group.

Statistical Methods[10,11,12,13]

Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean ± SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5 % level of significance. The following assumptions on data is made, Assumptions:

1. Dependent variables should be normally distributed,

2. Samples drawn from the population should be random, Cases of the samples should be independent

Student t test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups (Inter group analysis) on metric parameters.

Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups, Non-parametric setting for Qualitative data analysis. Fisher Exact test used when cell samples are very small.

Significant figures

+ Suggestive significance (p value: $0.05 < p < 0.10$)

* Moderately significant (p value: $0.01 < p \leq 0.05$)

** Strongly significant (p value: $p \leq 0.01$)

Statistical software: The Statistical software namely SPSS 18.0, and R environment ver.3.2.2 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc.

Results

Demographic Data

Seventy two patients were assessed for study , eight did not meet the inclusion criteria and 4 declined the block. 60 patients of either sex, belonging to ASA I, ASA II and ASA III undergoing elective ankle and foot surgeries were included in the study. All the patients were administered popliteal nerve block and were randomised into two groups: Group A and Group BN, to receive either 20ml of Inj Bupivacaine 0.5% with 1ml Normal Saline or 20ml of Inj Bupivacaine 0.5% with 1ml 10mg Nalbuphine respectively. There were no statistically significant differences between these groups in demographics and ASA grading.

Pre-Operative Vitals

The mean heart rate in Group S was 93.60 ± 11.11 and Group M was 86.20 ± 6.71. This was found to be statistically significant, with a p value of 0.003**. The mean SBP in Group S was 138.67 ± 22.97 and Group M was 140.80 ± 22.44. This was found to be statistically insignificant, with a p value of 0.717. The mean DBP in Group S was 89.33 ± 17.63 and Group M was 90.73 ± 14.81. This was found to be statistically insignificant, with a p value of 0.740 . The mean SpO_2 in Group L was 99.50 ± 0.90 and Group B was 99.67 ± 0.55. This was found to be statistically insignificant, with a p value of 0.381.

Post-Operative Vitals

The mean heart rate in Group S was 89.60 ± 10.65 and Group M was 81.27 ± 5.98. This was found to be statistically significant, with a p value of <0.001**. The mean SBP in Group S was 126.73 ± 23.51 and Group M was 131.53 ± 23.66. This was found to be statistically insignificant, with a p value of 0.434 . The mean DBP in Group S was 81.48 ± 14.68 and Group M was 85.13 ± 12.56. This was found to be statistically insignificant, with a p value of 0.316. The mean SpO_2 in Group L was 98.30 ± 0.90 and Group B was 98 ± 0.80. This was found to be statistically insignificant, with a p value of 0.177.

Table 1: Onset and duration of sensory block

	Group A	Group BN	p value
Onset of sensory block (in mins)	15.2 ± 1.8	11.8 ± 2.4	< 0.05
Duration of sensory block	552 ± 19	760 ± 23.3	< 0.05

Table 2: Onset and duration of motor block

	Group A	Group BN	p value
Onset of motor block (in mins)	17.6 ± 1.1	14.7 ± 1.5	< 0.05
Duration of motor block (in mins)	438 ± 18.4	573 ± 20.6	< 0.05

Discussion

In the field of anaesthesia there have been drastic changes with respect to inventions of various techniques and anaesthetic drugs however an

effective way to control pain postoperatively has still not been established. Various studies with unexplored techniques are now being done in an attempt to find the best methods for adequate anaesthesia and analgesia. We did a study titled "Effect of Nalbuphine as Adjuvant to Bupivacaine for Ultrasound-Guided Popliteal Nerve Block: A Prospective Randomised Comparative Clinical Study".

In our hospital based prospective, randomised comparative clinical study conducted on 60 patients undergoing Ankle and Foot surgeries at RajaRajeswari Medical College and Hospital between the time period from April 2017- January 2019, we randomised the patients by a simple sealed envelope method into Group A who received 20ml of Inj Bupivacaine 0.5% and 1ml of normal saline and Group BN who received 20ml of Inj Bupivacaine with 1ml 10mg Nalbuphine.

Popliteal nerve block for ankle and foot surgeries was found to be an excellent alternative to General and Spinal anaesthesia in achieving good intra operative conditions, longer post-operative analgesia with minimal adverse events.

Anaesthesia for Ankle and Foot Surgeries

Regional anaesthesia techniques are used frequently as an alternative to general anaesthesia in Ankle and Foot surgery. These surgeries are accompanied by pain for the first few days following surgery. Opioid based postoperative pain management can lead to inadequate pain relief and is accompanied by side effects.[1] Popliteal nerve block is a useful technique for ankle and foot surgeries, particularly in patients thought unsuitable for central neuraxial block. It also avoids complications in the elderly patients who are particularly prone for haemodynamic changes leading to increased morbidity and mortality.

Studies by Ayman A. El Sayed et al.[1]; Singelyn FJ, Gouverneur JM, Gribomont BF et al.[14] and R. Arcioni et al.[8] have shown an added advantage of popliteal nerve block in early post operative mobility which is essential in surgical procedures. It was determined that as a safe and reliable alternative to more common forms of anaesthesia for surgery below the knee and popliteal nerve block avoids post dural puncture headache, making it an ideal technique for ambulatory surgeries and can be used more readily after head injury where central neuraxial block is relatively contraindicated

In our study, we used a single injection lateral approach popliteal nerve block for all the patients posted for ankle and foot surgeries. It increased the patient's comfort and success rate, also decreased the adverse events.

Nalbuphine has been studied as an adjuvant to local anaesthetics in epidural, caudal, and intrathecal anaesthesia. Despite its known benefits for pain control very little data is available for its effects as an adjuvant to lower limb peripheral nerve blocks especially popliteal nerve block.

Nalbuphine is a synthetic mixed opioid agonist-antagonist with analgesic properties. Although its exact mechanism has not been fully delineated, it is hypothesized that upon administration, nalbuphine binds to kappa receptors in the central nervous system (CNS), thereby inhibiting the release of neurotransmitters that mediate pain, such as substance P.[15] Additionally, nalbuphine exerts post-synaptic inhibitory effects on interneurons and output neurons of the spinothalamic tract, responsible for transporting nociceptive information. Compared to other opioid agents that stimulate mu receptors, nalbuphine antagonises mu receptors, thereby potentially producing less intense respiratory depression.[9]

This study demonstrates that addition of 10 mg nalbuphine to bupivacaine in popliteal nerve block in patients undergoing ankle and foot surgeries decreases time of onset of anaesthesia, showssignificant increase induration of sensory and motor blockade and also increases the post operative analgesia.

Sensory blockade

In our study we found that Group BN patients who received Nalbuphine as additive provided faster onset of sensory level blockage with mean time of onset value being 11.8 ± 2.4 (in mins) compared to Group A where mean value was 15.20 ± 1.80 (in mins). The results were statistically significant with a p value of <0.001**. The duration of sensory level block in Group BN who received Nalbuphine as additive was 760 ± 23.3 compared to Group A where mean value was 552 ± 19 with statistically significant *p* value of <0.001**. With this result we can conclude that patients in Group BN had statistically significant more duration of sensory block when compared to Group A.

Our results were comparable to a study conducted by Mohamed Abdelhaq et al.[4] where addition of Nalbuphine prolongs the duration of action of sensory block when added to Inj Bupivacaine in Supra Clavicular Brachial Plexus Block.

In comparison to the study conducted by Gupta K, Jain M et al.[16] the addition of Nalbuphine to Bupivacaine in our study had a faster onset of action of sensory block.

Motor blockade

In our study we found that Group BN patients who received Nalbuphine as additive provided faster onset of motor level blockage with mean time of onset value being 14.7 ± 1.5(in mins) compared to Group A where mean value was17.6 ± 1.1(in mins). The results were statistically significant with a *p* value of <0.001**. The duration of motor level block in Group BN was 573 ± 20.6 compared to Group A where mean value was 438 ± 18.4with statistically significant *p* value of <0.001**. With this result we can conclude that patients in Group BN had statistically significant more duration of motor block when compared to Group A.

Our results were in agreement with a study conducted by Mohamed Abdelhaq et al.[4] where addition of Nalbuphine prolongs the duration of action of motor block in supraclavicular brachial plexus block.

Post Operative pain by VAS

Post operative pain, was measured by Visual Analogue Scale at intervals of 30 mins, at 2hrs, at 4hrs, at 6hrs, at 8hrs, at 12hrs and at 24hrs. For up to 6 hours after surgery the VAS for both the groups were similar with the values not being statistically significant. VAS was assessed again at 8 hours after surgery where Group A showed a mean VAS of 1.28 ± 0.45 and Group BN showed a mean VAS of 1.00 ± 0.00. This was statistically significant with a *p* value of 0.002**. At 12 hrs after surgery, Group A showed a mean VAS of 1.93 ± 0.37 and Group BN recorded a mean VAS of 1.07 ± 0.37. This was statistically significant with a *p* value of <0.001**. However, VAS assessed at 12 hours after surgery for both the groups were not statistically significant.

Analgesic requirement

In our study, the means of assessing postoperative analgesia was the time to first analgesic administration, the total amount of analgesic consumed in the first 24 hour period after surgery and the VAS at different time in first 24 hour. In both the groups all 60 patients did not ask for analgesia post operatively, since we assessed for pain only at rest and not on movement. Both the groups had excellent post operative analgesia with mean VAS scores of <4 even at 24 hours after surgery .

Rangel Vde O et al.[17] showed that the approach for tibial and common fibular nerves with single puncture in the popliteal fossa using peripheral nerve stimulator is a good option for anaesthesia and analgesia for foot surgeries.

Gallardo J et al.[18] conducted a study which showed that VAS evaluation had a significant improvement in pain control in the group with the popliteal block after 6, 12, 18, and 24 hours post surgery, with pain levels peaking and being most different between 6 and 12 hours post surgery and also exhibited a significantly lower consumption of morphine and a greater degree of patient satisfaction.

We completely agree with Gallardo J et al.[18] because in our study VAS evaluation had a significant pain control in both groups up to 12 hours and patients from both the groups showed a high rate of satisfaction with the procedure and demonstrated a good discharge disposition. No significant difference in satisfaction could be detected between the 2 groups in the study. We also did not observe any anaesthesia related complications in all the 60 patients who underwent popliteal nerve block for the proposed surgical procedures.

Limitations

1. The small sample size is a limitation of this study, however performing the blockade with the patient awake and with the use of a nerve stimulator explains the absence of neurological problems and the few complications reported in the literature
2. Plasma levels of nalbuphine doses used were safe and effective. We need to find minimal doses in order to optimise the doses effectively for the adjuvants.
3. An apparent disadvantage of popliteal nerve block was longer intervention duration, which could easily be resolved by performing the intervention in the patient premedication room.

Conclusion

This study demonstrates that addition of 10mg Nalbuphineto Bupivacaine in popliteal nerve block in patients undergoing ankle and foot surgeries :

1. Decreases time of onset of anaesthesia
2. Shows significant increase in duration of sensory and motor blockade
3. Increases the post operative analgesia

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