The effect of addition of local or intravenous ketorolac and morphine as an adjuvant to local anesthetic in popliteal nerve block. A comparative study with epidural anesthesia for foot or ankle surgery in diabetic patient

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Abstract:

Aim: The aim is to study the effect of addition of ketorolac and morphine as an adjuvant to local anesthesia in popliteal nerve block in comparison with epidural anesthesia for foot or ankle surgery in diabetic patients

Patients and method: The study was done on 90 diabetic patients ASA II, III scheduled foot or ankle surgery Patients were randomly allocated into 3 equal groups (30 patients in each group):

Group I: received epidural anesthesia.

Group II: received popliteal nerve block (posterior approach) contains 0.5% plain bupivacaine plus morphine 2 mg +ketorolac 30 mg (Total volume 30 ml).

Group III: received popliteal nerve block (posterior approach) contains 0.5% plain bupivacaine (Total volume 30 ml) plus I.V. morphine 2 mg +ketorolac 30 mg.

The following parameters were recorded: (1) Onset of block. (2) Analgesia duration. (3) Early mobilization. (4) Time for hospital discharge. (5) Side effects.

Results: : Group II has decreased onset of block, long duration of analgesia, early mobilization, less hospital discharge time and less side effects in comparison with groups I and III.

Conclusion: Popliteal nerve block with local adjuvants (Morphine and ketorolac) compared with epidural analgesia results in decreased onset, faster mobilization, and earlier time for hospital discharge with minimal side effects. Ketorolac and morphine are more efficient when given locally than systemically.

Introduction:

Patients with long duration of diabetes are more prone for multi system disorders and compromised physiological state. Diabetic foot surgeries are mostly performed under regional nerve blockade, which does not interfere much with normal physiology [(1)]. The desire to improve postoperative pain control and reduce postoperative narcotic medication use following foot and ankle surgery has led to recent increased interest in regional blocks to

the sciatic nerve [2]. Ankle blocks, which are more commonly used, are an effective means of pain control. However, due to the limited volume of anesthetic that can be injected, their duration is comparatively short [3]. Labat [4] first described blocking the sciatic nerve through the popliteal fossa in 1923. The sciatic nerve (L4 and L5, S1 through S3) is the largest of the four peripheral nerves of the lower extremity. The sciatic nerve is composed of two nerves bound by a common sheath of connective tissue; the tibial component is medial and anterior, and the common peroneal component is lateral and slightly posterior. After passing through the sacrosciatic foramen beneath the piriformis muscle, it lies between the greater trochanter of the femur and the ischial tuberosity. The nerve becomes superficial at the lower border of the gluteus maximus muscle, where it begins its descent down the posterior aspect of the thigh to the popliteal fossa. It supplies cutaneous innervation to the posterior of the thigh and all of the leg and foot below the knee, except for a thin medial strip supplied by the saphenous nerve [17].

Popliteal block is a rapid, effective and safe anesthesia for foot surgery or for pain relief after foot surgery. In this block the sciatic nerve is blocked in the area of the popliteal fossa. Popliteal sciatic nerve block has the advantage over more proximal sciatic blocks of preserving hamstring function and allowing early ambulation with crutches [5]. Compared with regional anesthesia, it results in a unilateral block, carries no risk of postdural puncture headache, results in prolonged postoperative analgesia, and can be performed in patients being treated with anticoagulant therapy [6].

The discovery of peripheral opioid receptors offers yet another circumstance in which co administration of local anesthetic with opioid may be useful [18]. The most promising clinical results have been from intra-articular administration local anesthetic and opioid for post operative analgesia [19]. Although intravenous opioids alone can produce excellent post-operative analgesia, many patients experience significant dose-dependent side effects. When local anesthetic solutions are combined with opioids, significant synergy is observed. Bupivacaine combined with morphine provides excellent analgesia with lower drug requirements and fewer side effects. Addition of ketorolac enhances and prolongs analgesia and may reduce systemic absorption of opioids [8].

Ketorolac is a parenterally administered non-steroidal anti-inflammatory drug (NSAID) that provides analgesia by inhibiting prostaglandin synthesis. Ketorolac is indicated for the short-term (less than 5 days) management of pain, and appears to be particularly useful in the immediate postoperative period. A standard dose of ketorolac provides analgesia equivalent to 6–12 mg of morphine administered by the same route. It's time to onset is also similar to morphine, but ketorolac has a longer duration of action (6–8 h). Ketorolac, a peripherally acting drug, has become a popular alternative to opioids for postoperative analgesia because of its minimal central nervous system side effects. Specifically, ketorolac does not cause respiratory depression, sedation, or nausea and vomiting. In fact, ketorolac does not cross the blood–brain barrier to any significant degree. Numerous studies have shown that oral and parenteral NSAIDs have an opioid-sparing effect [7].

Patients and methods:

After obtaining institutional ethical committee approval and written informed consent. 90 diabetic patients ASA II, III scheduled foot or ankle surgery. Planned surgery that would cause pain outside the distribution of the sciatic nerve (e.g., iliac crest bone graft), revision surgery, inability of the patients to describe postoperative pain to the investigators (language barrier, psychiatric disorder, or dementia), coagulopathy, contraindications to any of the performing medications and contraindications to any of the following: performance of popliteal fossa nerve block, performance of neuraxial anesthesia were excluded from the study. After intravenous access, a combination of midazolam (1 mg) and fentanyl (30 µg) are given to provide amnesia, sedation and analgesia for the placement of the blocks.
Patients were randomly allocated into 3 equal groups (30 patients in each group):
Group I: received lumber epidural anesthesia using 0.5% plain bupivacaine 1:2 ml per segment. The level of anesthesia was kept between T_{10} and T_{12}.
Group II: received popliteal nerve block (posterior approach) contains 0.5% plain bupivacaine plus morphine 2 mg +ketorolac 30 mg (Total volume 30 ml).
Group III: received popliteal nerve block (posterior approach) contains 0.5% plain bupivacaine (Total volume 30 ml) plus I.V. morphine 2 mg +ketorolac 30 mg.
The posterior approach of the popliteal nerve block was performed with patients in the prone position. With the leg fully extended, a 100 mm insulated needle attached to a nerve stimulator (set at a frequency of 2 Hz, pulse width 100 µs, and current intensity 1.5 mA) was inserted perpendicular at the midpoint between the tendons of the biceps femoris and semitendinosus muscles, 7 cm above the popliteal fossa crease. The needle was advanced slowly while a plantar or dorsiflexion of the foot or toes was sought. If there was failure to stimulate the sciatic nerve, removal of the needle and repetition of the same maneuvers through a new puncture site 5-mm lateral to the initial insertion site was done (second attempt). This technique was repeated through new insertion sites (subsequent attempts) in 5-mm incremental lateral insertions until the desired response was obtained. The needle position will be considered acceptable if an evoked motor response of the ipsilateral foot is elicited at $\leq$0.5 mA.
The following parameters were recorded: (1) **Onset of block** was defined as time from administration of the block to complete disappearance of sensation in the distribution of the block(2) **Analgesia duration** was defined as time from administration of the block to return of pain, as reported by the patient, determined by patient interview. (3) **Early mobilization.** (4) Time for **hospital discharge**. (5) **Side effects** (Nausea, vomiting, dysesthesia, neuropraxia, hypotension and bradycardia). Dysesthesia was defined as any abnormal sensation in the distribution of the sciatic nerve, most commonly described as tingling or "pins and needles" sensation after cessation of block. Neuropraxia was defined as an objective abnormality of the neurologic examination in the distribution of the sciatic nerve on the operative side. Hypotension was defined as 30% decrease of main blood pressure below the original level. Bradycardia was defined as heart rate below 60 beat/min.

Statistical analysis:

The collected data will be tabulated and analyzed using Statistical Package of Social Science (SPSS) version 16. Suitable statistical techniques were computed (mean, standard deviation, chi square test, and ANOVA test).

Results:

-Patient demographic data show non-significant difference among the three groups as regard age, body weight, height, ASA physical status and body mass index (Table 1).

Table (1): Demographic data:

	Group I	Group II	Group III	F- value	P- value
Age(years)	48.20± 14.936	47.75± 14.227	47.55± 14.148	2.7	>0.05
BW(kg)	79.80± 18.063	70.45± 18.805	64.75± 22.833	2.9	>0.05
HT(Cm)	167.60± 13.843	167.25± 13.591	167.20± 13.387	2.6	>0.05
ASA	2.10± .718	1.80± .768	1.95± .686	0.9	>0.05
BMI	27.29 ± 2.356	27.29 ± 2.356	27.29 ± 2.356	2.7	> 0.05

P > 0.05 not significant P <0.05* significant

-As regard the onset of block group II shows statistically highly significant short onset of action (11.8 min.±3.8) in comparison with group I (19.83 min.±6.6) and group III (15.8 min.±5.16) (F value : 47.6, P value<0.001) **(table 2) (fig. 1).**
-As regard the analgesia duration group II shows statistically highly significant prolongation of block duration (18.3 hr.±5.8) in comparison with group I (13.8 hr.±6.6) and group III (14.8 hr.±7.2) (F value : 19.1, P value<0.001) **(table 2) (fig. 1).**
-As regard the early mobilization there is statistically highly significant decrease in mobilization time in groups II (16.3 min.±5.3) and III (30.4 min.±9.93) in comparison with group I (111.34 min. ±37.096).Also there is statistically significant difference between group II and group III (F value: 3270.4,P <0.001) **(table 2) (fig. 1).**
-As regard the time for hospital discharge there is statistically highly significant decrease in hospital discharge time in groups II (120.3 min.±38.3) and III (125.4 min.±31.25) in comparison with group I (361.34 min. ±120.36) (F value: 12146.5, P <0.001) **(tab. 2) (fig.1).**

Table (2)

	Group I	Group II	Group III	F- value	P- value
Block onset (min)	19.83±6.6	11.8±3.8	15.8±5.16	47.6	<0.001
Analgesia duration(Hours)	13.8 ±6.6	18.3 ±5.8	14.8 ±7.2	19.1	<0.001
Early mobilization(min.)	111.34±37.096	16.3±5.3	30.4±9.93	3270.4	<0.001
hospital discharge(min.)	361.34±120.36	120.3±38.3	125.4±31.25	12146.5	<0.001

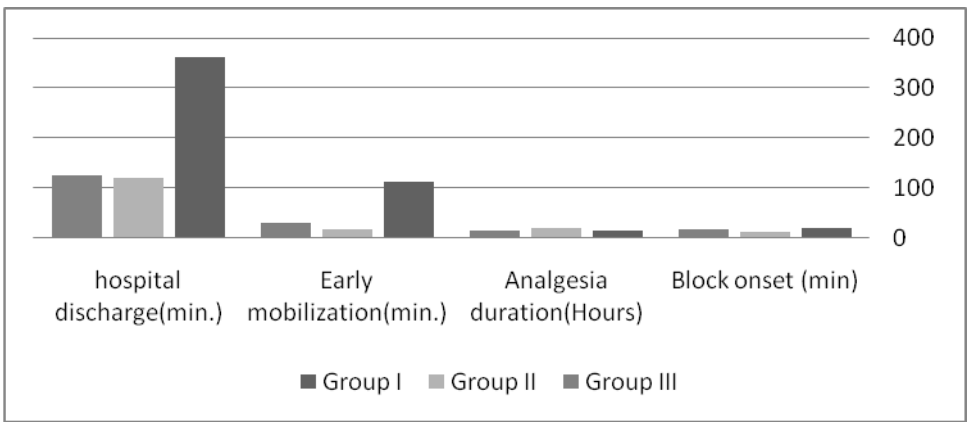

Figure 1

-As regard the side effects (Table 3) (Figure 2):

* **Nausea**: Only 3 patients (10%) of Group II developed nausea while 10 patients (33.3%) of group I and 13 patients (43.3%) of Group III which is statistically significant (F value: 8.5,P <0.05).

* **Vomiting**: Only one patient (3.3%) in Group II developed vomiting while 4 patients (13.3%) in group I and 8 patients (26.7%) in group III which is statistically significant (F value: 7.5,P <0.05).

* **Dysesthesia**: Only 2 patients (6.6%) in group II developed dysesthesia which is statistically significant than group I (8 patients) (26.6%) and group III (10 patients) (30%) (F value: 6.7, P <0.05).

* **Neuropraxia**: Only 1 patient in group III developed neuropraxia.

* **Hypotension**: Only 5 patients in group I developed hypotension treated with I.V. infusion of crystalloids.

* **Bradycardia**: Only 4 patients in group I and 1 patient in group III developed bradycardia treated with I.V. atropine 0.1 mg/kg.

Table (3): Side effects:

	Group I	Group II	Group III	F- value	P- value
Nausea	10(33.3%)	3 (10%)	13 (43.3%)	8.5	<0.05
Vomiting	4 (13.3%)	1(3.3%)	8 (26.7%)	7.5	<0.05
Dysesthesia	8(26.6%)	2 (6.6%)	10 (30%)	6.7	<0.05
Neuropraxia	0	0	1	2.02	>0.05
Hypotension	5	0	0	10.6	<0.05
Bradycardia	4	0	1	5.5	>0.05

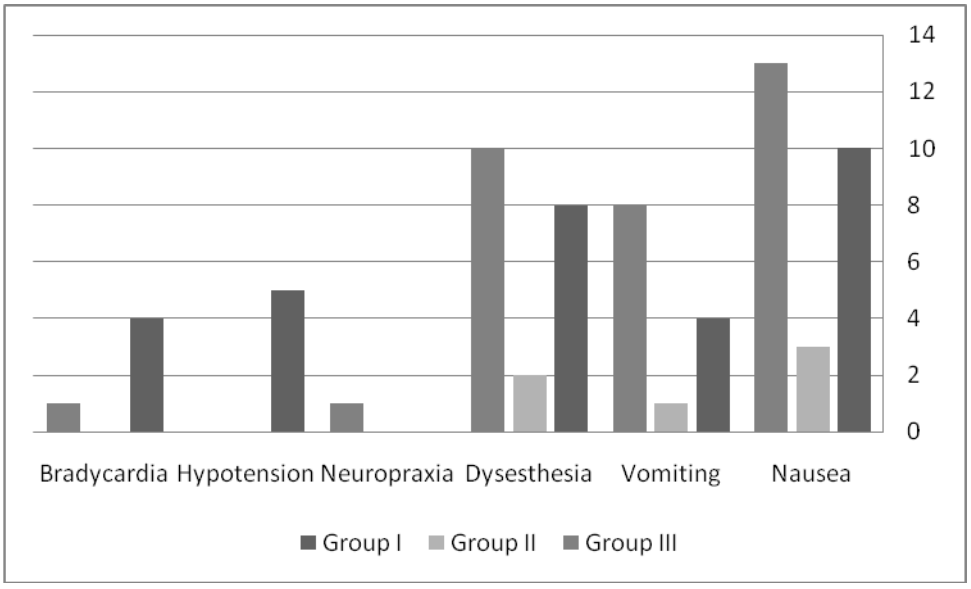

Figure 2

Discussion:

This study demonstrated that addition of ketorolac and morphine to bupivacaine significantly decreases the onset of action and prolonged the analgesia obtained from popliteal fossa nerve blockade compared with epidural anesthesia and when both drugs are given intravenously. Thus, addition of ketorolac and morphine to the local anesthetic solution can be recommended when performing popliteal fossa nerve block with bupivacaine. No major side effects were noted from this technique. Many authors [8, 9, 10] suggesting that the administration of local anesthetic–opioid mixtures neuraxially (particularly epidural) or locally is an excellent technique for managing postoperative pain following surgery. Patients often have better preservation of pulmonary function, are able to ambulate early, and benefit from early physical therapy. Moreover, patients may be at lower risk for postoperative venous thrombosis. Chelly [20] and his colleagues demonstrate that the addition of 3 to 5 mg of morphine to the local anesthetic mixture can prolong the duration of analgesia up to 36 hours. The combination of 0.1 mg/kg of morphine and lidocaine injected locally can reduce by 50% the total dose of morphine required for postoperative analgesia which is goes with our results.
The present study used 30 cc of bupivacaine 0.5% which is goes with Jacques et al, [11] who tested the hypothesis that increasing the concentration of bupivacaine from 0.375 to 0.75% would increase the duration of postoperative analgesia by 3 h. after foot or ankle surgery. Patients were randomly assigned to receive a popliteal fossa block (posterior approach) using 30 cc of either 0.375% or 0.75% bupivacaine and found that there was no benefit to increasing the concentration of bupivacaine above 0.375% for single-injection popliteal fossa nerve blockade when performed for postoperative analgesia. A volume of 30 to 45 ml of local anesthetic solution is used in popliteal nerve blockade by many authors [13, 14]. Jerry et al, [15] also favors larger volumes of local anesthetics for this block, because the large content of fat in the popliteal fossa and a thick epineurium of the sciatic nerve may decrease the amount of local anesthetic that reaches the nerve and thus adversely affect the success of popliteal nerve block. It additionally, larger volumes of local anesthetic also may extend the duration of action of the block and play a role in optimizing postoperative pain relief. [16]

The technique used for the present study is single injection posterior approach which was chosen according to the study done by Xavier et al, [12] who compared single-injection and double-injection of the sciatic nerve with nerve stimulation in the posterior popliteal approach using mepivacaine 1% in a prospective, randomized and single-blind study to evaluate effectiveness, delay of onset, and complications in patients undergoing foot and ankle surgery and they conclude that double-nerve stimulation of the sciatic nerve gives similar complete onset times and overall success rate to single-nerve stimulation and more paresthesias during block performance.

Many additives are added to narcotics to decrease the amount of narcotics needed and provide effective pain relief. Ketorolac is one of these additives. It is thought that blocking the effects of prostaglandins is what makes ketorolac useful for reducing pain. In clinical studies, ketorolac was as effective as lower doses of narcotics at treating pain. When it was combined with narcotic pain medicines such as morphine, it decreased the amount of narcotics needed. Also, pain relief was significantly better in those receiving ketorolac and morphine compared to those receiving morphine alone [22]. Jason et al, [21] studied the effect of spinal morphine and ketorolac and selective COX_1 and COX_2 inhibitors in nerve injuries without any neurotoxic effect on the spinal cord which indicate that ketorolac is safe when applied locally.

In conclusion, popliteal nerve block with local adjuvants (Morphine and ketorolac) compared with epidural anesthesia results in decreased onset, prolonged analgesia, faster mobilization, and earlier time for hospital discharge with minimal side effects. Ketorolac and morphine are more efficient when given locally than systemically. It considered a good alternative in patient with coagulation disorders.

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