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SCIENTIFIC ARTICLE

Comparison of tramadol and lornoxicam in intravenous regional anesthesia: a randomized controlled trial

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Abstract
Background and objectives: Tourniquet pain is one of the major obstacles for intravenous regional anesthesia. We aimed to compare tramadol and lornoxicam used in intravenous regional anesthesia as regards their effects on the quality of anesthesia, tourniquet pain and postoperative pain as well.

Methods: After the ethics committee approval 51 patients of ASA physical status I–II aged 18–65 years were enrolled. The patients were divided into three groups. Group P ($n = 17$) received 3 mg/kg 0.5% prilocaine; group PT ($n = 17$) 3 mg/kg 0.5% prilocaine + 2 mL (100 mg) tramadol and group PL ($n = 17$) 3 mg/kg 0.5% prilocaine + 2 mL (8 mg) lornoxicam for intravenous regional anesthesia. Sensory and motor block onset and recovery times were noted, as well as tourniquet pains and postoperative analgesic consumptions.

Results: Sensory block onset times in the groups PT and PL were shorter, whereas the corresponding recovery times were longer than those in the group P. Motor block onset times in the groups PT and PL were shorter than that in the group P, whereas recovery time in the group PL was longer than those in the groups P and PT. Tourniquet pain onset time was shortest in the group P and longest in the group PL. There was no difference regarding tourniquet pain among the groups. Group PL displayed the lowest analgesic consumption postoperatively.

Conclusion: Adding tramadol and lornoxicam to prilocaine for intravenous regional anesthesia produces favorable effects on sensory and motor blockade. Postoperative analgesic consumption can be decreased by adding tramadol and lornoxicam to prilocaine in intravenous regional anesthesia.

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Comparação de tramadol e lornoxicam em anestesia regional por via intravenosa, um estudo randomizado e controlado

Resumo

Justificativa e objetivos: A dor relacionada ao torniquete é um dos maiores obstáculos para a anestesia regional intravenosa (ARIV). Nosso objetivo foi comparar tramadol e lornoxicam usados em ARIV em relação aos seus efeitos sobre a qualidade da anestesia, dor relacionada ao torniquete e dor no pós-operatório.

Métodos: Após a aprovação do Comitê de Ética, 51 pacientes com estado físico ASA I–II e idades entre 18–65 anos foram inscritos. Os pacientes foram divididos em três grupos. Grupo P (n = 17) recebeu 3 mg/kg de prilocaína a 0,5%; Grupo PT (n = 17) 3 mg/kg de prilocaína a 0,5% + 2 mL (100 mg) de tramadol e Grupo PL (n = 17) de 3 mg/kg de prilocaína a 0,5% + 2 mL (8 mg) de lornoxicam para ARIV. O início do bloqueio sensorial e motor e os tempos de recuperação foram registrados, bem como a dor relacionada ao torniquete e o consumo de analgésico no pós-operatório.

Resultados: Os tempos de início do bloqueio sensorial foram mais curtos nos grupos PT e PL, enquanto que os tempos de recuperação correspondentes foram mais longos que os do Grupo P. Os tempos de início do bloqueio motor nos grupos PT e PL foram menores que no Grupo P, enquanto que o tempo de recuperação do grupo PL foi maior que os dos grupos P e PT. O tempo para início da dor relacionada ao torniquete foi menor no Grupo P e maior no Grupo PL. Não houve diferença em relação à dor relacionada ao torniquete entre os grupos. O Grupo PL apresentou o menor consumo de analgésicos no pós-operatório.

Conclusão: A adição de tramadol e lornoxicam à prilocaína para ARIV produz efeitos favoráveis sobre o bloqueio sensorial e motor. O consumo de analgésicos no pós-operatório pode ser reduzido com a adição de tramadol e lornoxicam à prilocaína em ARIV.

Introduction

Intravenous regional anesthesia (IVRA), commonly named a Bier Block, has been introduced in 1908 by Karl August Bier.[1] Ease of application of the method, fast onset of anesthesia, lower cost compared with general anesthesia and no need for deep sedation makes the Bier Block a method of choice for surgical procedures on extremities lasting less than an hour.[2,3] IVRA can be used for emergency operations on extremities for the patients with full stomach. It has a success rate of 96%–100% for upper extremity and is a good alternative for peripheral nerve block.[4,5] Compared with general anesthesia IVRA shortens hospital length of stay, necessitates 30% less nurse care and 84% less drug need.[6]

Because of the high potential of systemic toxicity bupivacaine and etidocaine are not preferred for IVRA. Lidocaine and prilocaine are the most commonly used local anesthetics for this. Prilocaine metabolism is the fastest among all local anesthetics.

One of the most important factors preventing the use of IVRA is tourniquet pain. Many adjuvant drugs have been used to decrease the tourniquet pain, increase anesthesia quality and decrease postoperative pain. Among these are tramadol, ketorolac, lornoxicam, clonidine, dexamethasone, paracetamol.[7–9]

We aimed in our study to compare the effects of tramadol and lornoxicam added to prilocaine for IVRA for patients undergoing upper extremity surgery.

Methods

Fifty-one patients of ASA physical status I and II, aged 18–65 years old undergoing hand and wrist surgery (carpal tunnel release, tendon repair, phalanx fracture repair, cystic hygroma, dupuytren contracture repair) were enrolled in the study after clinical trials ethical committee approval (T.C. Ankara Valiliği İl Sağlık Müdürlüğü, 12.05.2009, n° 051920). The study was conducted in the Ankara Numune Research Hospital in 2009. Written informed consent was taken from all the patients.

Patients were premedicated by midazolam 0.15 mg/kg and atropine 0.01 mg/kg given intravenously from iv line opened on the antecubital side of the non-operative arm 5 mL/kg/h isotonic physiologic saline solution was started afterwards. In the operation room 24 gauge iv line was placed on the dorsal part of the arm that will undergo operation. Routine monitorization included non-invasive blood pressure (NIBP), electrocardiography (ECG) and peripheral oxygen saturation (SpO$_2$). Extremity that will undergo operation was elevated for 3 min before application of Esmarch bandage. After the application of bandage the proximal cuff of the double-cuffed tourniquet (Tourniquet 2800 ELC, UMB Medizintecknik, GmbH, Germany) was inflated 100 mmHg above the systolic arterial pressure of the same extremity (to at least 250 mmHg). Esmarch bandage was removed after the inflation of the tourniquet. Existence of the occlusion pressure was confirmed by cessation of the radial pulse and pulse oximetry trace.

Table 1 Demographic characteristics.

	Group P(n = 17)	Group PT(n = 17)	Group PL(n = 17)	p
Age (years)	38.7 ± 15.3	37.8 ± 13.4	38.2 ± 12.6	0.981
Sex (male/female)	8/9	10/7	8/9	0.731
Body weight (kg)	71.4 ± 7.6	69.5 ± 6.6	74.9 ± 8.8	0.128
Height (cm)	170.9 ± 4.3	171.1 ± 5.1	171.5 ± 6.8	0.940
Body mass index (kg/m^2)	24.4 ± 2.4	23.8 ± 2.6	25.4 ± 2.4	0.157
ASA (I/II)	9/8	9/8	7/10	0.731
Operation time (min)	40.3 ± 11.2	40.0 ± 9.8	41.3 ± 9.3	0.940

Patients were randomized into three groups by the closed envelope system. Group P (n = 17) received 3 mg/kg 0.5% prilocaine (Citanest, Astrazeneca), group PT (n = 17) received 3 mg/kg 0.5% prilocaine + 2 mL (100 mg) tramadol (Contramal, Abdi İbrahim) and group PL (n = 17) received 3 mg/kg 0.5% prilocaine + 2 mL (8 mg) lornoxicam (Xefo, Nycomed) for IVRA.

The drug solutions were applied by the anesthesiologist from the iv line on the extremity that will be operated throughout 90 s period. After the application of the solution sensory blockade onset time was evaluated by pinprick testing from the median, radial and ulnar dermatomes every 30 s. Sensory blockade onset time was noted as the time from the finishing of the drug solution injection to the time that all dermatomes of the arm and forearm are negative for pinprick testing. Motor blockade onset time was noted as the time from the finishing of the drug solution injection to the time that none of the fingers on the hand can move. A sensory block assessment was done by Visual Analog Scale (VAS). Modified Bromage Scale was used for motor block assessment of the extremity. After the sensory block onset on all the extremities the proximal tourniquet was deflated after the inflation of the distal tourniquet and operation was started.

Tourniquet pain was noted as before tourniquet inflation (BT), at the 5th, 10th, 20th and 30th minutes of tourniquet (T 5, T 10, T 20, T 30) and at the 15th, 30th and 60th minutes after the tourniquet deflation (AT 15, AT 30, AT 60). Fentanyl was used as a rescue analgesic during the operation and the dose was noted. All the side effects during the anesthesia and surgical procedure were noted.

Tourniquet time was kept between 30 and 90 min range regardless of the duration of the operation. After the deflation of the tourniquet, time to the positive pinprick test on median, radial and ulnar dermatomes was noted as sensory block recovery time and time to the start of the movement of the fingers was noted as motor block recovery time. Patients were followed-up for 60 min in the post-anesthesia care unit and VAS scores for tourniquet pain were noted on 15th, 30th and 60th minutes. Diclofenak sodium (Voltaren, Ciba Geigy)

75 mg im was used as a rescue analgesic postoperatively and 24 h analgesic consumption was noted. All the side effects, if any, were noted.

Statistical evaluation was done using SPSS 11.5 software. Student's t tests were used for comparisons of data which are commonly expected to be normally distributed, e.g. demographics, time of the onset and recovery of sensory and motor block, duration of the operation and tourniquet, duration of analgesia, and intraoperative and postoperative analgesic use. The Kruskal–Wallis test was used for intraoperative and postoperative VAS. Significance was assumed at $p \leq 0.05$. Using pooled data from previous IVRA lornoxicam/lidocaine and tramadol/lidocaine studies, we calculated that a sample size of 15 patients would permit a Type I error of $\alpha = 0.05$ and a power of 80%.

Results

There was no statistically significant difference between the groups regarding demographic characteristics and operation times ($p > 0.05$) (Table 1).

Sensory block onset times in groups PT and PL were shorter than that in group P. This difference was statistically significant ($p < 0.001$). Although the sensory block onset time in group PL was shorter than that in group PT, this difference was not statistically significant.

Sensory block recovery times in groups PT and PL were longer than that in group P. This difference was statistically significant ($p < 0.001$). Sensory block recovery time in group PL was longer than that in group PT and this difference was statistically significant ($p < 0.001$) (Table 2).

Motor block onset times in groups PT and PL were shorter than that in group P, this difference was statistically significant ($p < 0.001$). Although the motor block onset time in group PL was shorter than that in group PT, this difference was not statistically significant.

Motor block recovery time in group PL was longer than that in groups P and PT and this difference was statistically significant ($p < 0.001$) (Table 3).

Table 2 Sensory block onset and recovery times.

	Group P	Group PT	Group PL	p
Sensory block onset time (min)	8.0 ± 0.68	6.0 ± 1.17	5.5 ± 0.77	<0.001[a]
Sensory block recovery time (min)	4.6 ± 0.70	5.2 ± 0.77	6.9 ± 1.06	<0.001[a]

[a] $p < 0.05$.

Table 3 Motor block onset and recovery times.

	Group P	Group PT	Group PL	p
Motor block onset time (min)	11.9 ± 1.11	9.1 ± 0.67	8.8 ± 0.98	<0.001[a]
Motor block recovery time (min)	5.1 ± 1.20	4.6 ± 1.34	7.9 ± 1.34	<0.001[a]

[a] $p < 0.05$.

Table 4 Tourniquet pain and fentanyl consumption.

	Group P	Group PT	Group PL	p
Distal tourniquet time (min)	45.3 ± 11.2	45.6 ± 9.5	46.3 ± 9.3	0.963
Patients with tourniquet pain	10 (58.8%)	4 (23.5%)	9 (52.9%)	0.086
Tourniquet pain onset time (min)	32.5 ± 4.9	33.7 ± 7.5	39.2 ± 7.3	0.081
Patient number needing intraoperative fentanyl	9 (52.9%)	3 (17.6%)	8 (47.1%)	0.078
Intraoperative fentanyl consumption (μg)	66.7 ± 25	50 ± 0	50 ± 0	0.129

BT : Before touniquet
T : Tourniquet time
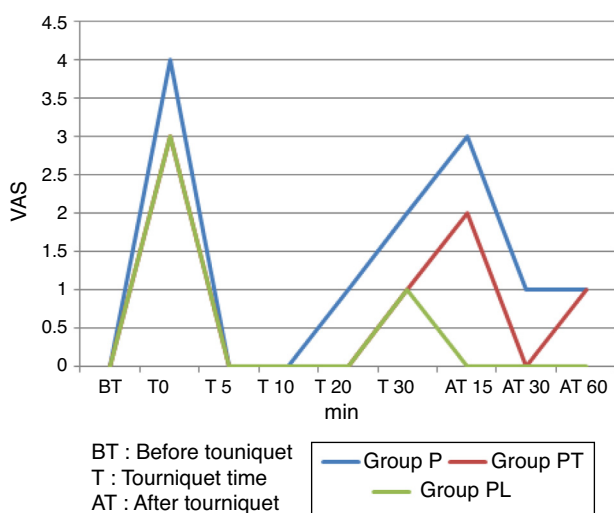AT : After tourniquet

— Group P — Group PT — Group PL

Figure 1 Tourniquet pain VAS scores.

There was no statistically significant difference among the groups as regards the tourniquet times. The tourniquet pain onset time was shortest in group P and longest in group PL, but this difference was not statistically significant ($p > 0.05$). Rescue fentanyl need was lowest in group PT, but again this difference was not statistically significant ($p > 0.05$) (Table 4).

Patients' tourniquet pain VAS scores are given in Fig. 1. There was no statistically significant difference among the groups ($p > 0.05$).

Table 5 Postoperative analgesic consumption for 24 h.

Postoperative diclorone consumption	Yes	No	p
Group P	14 (82.4%)	3	0.018[a]
Group PT	11 (64.7)%	6	
Group PL	6 (35.3%)	11	

[a] $p < 0.05$.

Table 5 illustrates the 24 h analgesic consumption of the patients. There was statistically significant difference among the groups regarding postoperative diclorone consumption ($p < 0.05$). Group PL displayed the lowest consumption of diclorone.

None of the patients experienced any side effects regarding local anesthetic toxicity.

Discussion

The main outcome of our study was that postoperative analgesic consumption was markedly less in the group where lornoxicam was added to prilocaine. In the groups with tramadol and lornoxicam sensory block onset times were shorter and recovery times were longer. Again, in the groups with tramadol and lornoxicam motor block onset times were shorter, whereas in the group with lornoxicam motor block recovery time was markedly longer.

Tan et al.[10] have observed shorter onset of sensory and motor block and less tourniquet pain with tramadol 50 mg added to lidocaine for IVRA, even if it was statistically insignificant.

Acalovschi et al.[11] have reported significantly shorter onset time of sensory block with tramadol added for IVRA. In the group with tramadol they have displayed longer recovery times for touch sensation. They attributed the inability of tramadol to make changes on the motor block on its low concentration. They speculated that tramadol used in low concentrations affects small nerves and nerve endings and higher concentrations should be used to affect nerve trunks. They used tramadol in 0.25% concentration. But Kapral et al.[12] have displayed that tramadol in 0.25% concentration added to mepivacaine for brachial plexus blockade prolongs the duration of sensory and motor block. Tramadol may have different pharmacodynamics in IVRA and brachial plexus blockade. In brachial plexus blockade anesthetic agents penetrate mixed nerves simultaneously, whereas in IVRA the first effect place is nerve endings followed by nerve trunks.[13] Langlois et al.[14] have used lidocaine 3 mg/kg with tramadol 100 mg for IVRA and observed no positive effect on postoperative analgesia. We observed in our study that adding

tramadol to prilocaine prolongs tourniquet pain onset time and reduces fentanyl need during the operation.

Sen et al.[15] used lornoxicam for IVRA and found shorter sensory and motor block onset times. They have displayed increased tourniquet tolerance, faster onset and better quality of anesthesia, less analgesic consumption during and after the operation without any side effects with lornoxicam added to lidocaine for IVRA. Our findings are compatible with these. We also observed less fentanyl consumption in the group with tramadol, even though the difference was not statistically significant.

Kol et al.'s[9] study was the only study investigating lornoxicam added to prilocaine for IVRA in the literature. This study has demonstrated longer sensory and motor block recovery times, longer analgesia and tourniquet tolerance times with lornoxicam added for IVRA. 24 h analgesic consumption was also less in the group with lornoxicam. Our findings were coherent with these.

As it is known, local anesthetic drugs have specific pK_a and pH of IVRA solution can be increased to approximate physiological pH, thus showing more permeability through the cell membrane resulting in faster onset of action of local anesthetics.[15,16] Sen et al.[15] measured pH of lidocaine 6.7, lornoxicam 8.7 and lornoxicam–lidocaine mixture to be 7.6. They have stated that the faster onset of sensory and motor blockade may have been attributed to the alkalinization of the local anesthetic solution by adding lornoxicam. We have not measured the pH values of the drugs used in our study, but we know that pH of prilocaine is 6.9 and of lornoxicam is 8.7. We think, similar to Sen et al., that addition of lornoxicam may have increased the pH value of prilocaine resulting in faster onset of sensory and motor block.

Sen et al.[15] stated that prolonged motor block of the extremity can prevent the distribution of local anesthetic into the systemic circulation, thus preventing local anesthetic toxicity. We have observed prolonged motor block in groups with tramadol and lornoxicam compared with the control group. No findings of systemic toxicity of local anesthetics have been observed in our study and we are in agreement with Sen et al.'s opinion.

Reuben and Duprat[17] have demonstrated that non-steroidal anti-inflammatory drugs (NSAID) decrease afferent nociceptive signals and inflammatory mediators from the surgical field. The effect of NSAIDs is thought to be through cyclooxygenase-2 (COX-2) enzyme inhibition, but other mechanisms may have been involved. NSAIDs may inhibit the conductance of C-fibers which are involved in propagation of tourniquet pain impulses.[18] Besides this, some NSAIDs exhibit their peripheral antinociceptive actions through K$^+$ channels.[18] Activation of NO-cGMP pathway may also induce antinociception through K$^+$ channels.[18,19] Positive effects of NSAIDs like lornoxicam or ketorolac on analgesia when used for IVRA are thought to be through a mechanism other than COX-2 inhibition.[15,20] Ischemia and oxidative stress have also been blamed in tourniquet pain.[21] Lornoxicam was found to have antioxidative effects on rats,[22] thus its positive effects on tourniquet pain can be attributed to its antioxidative properties. Jankovic et al.[20] have stated that analgesic properties of NSAIDs may be due to their antioxidant properties. Kanbak et al.[23] have compared ketorolac and tenoxicam for IVRA and found tenoxicam to be better as regards tourniquet pain. They related this phenomenon to the antioxidative properties of tenoxicam.

In our study 14 (82.4%) patients in group P, 11 (64.7%) patients in group PT and only 6 (35.3%) patients in group PL needed rescue analgesics during the first 24 h period postoperatively. Lornoxicam provided better analgesia postoperatively compared with tramadol. Optimal dose of lornoxicam for IVRA is not known. We used routine iv dose in our study. Steinberg et al.[24] have displayed that 20 mg ketorolac used for IVRA is as effective as 60 mg. Possible mechanisms for this are high concentration of the drug in the surgical field,[24] binding of the drug to the local tissue or long stay in the surgical field.[25] Studies identify an optimal dose of lornoxicam for IVRA can be performed.

Conclusions

In conclusion, adding tramadol and lornoxicam to prilocaine for IVRA produces favorable effects on sensory and motor blockade. Postoperative analgesic consumption can be decreased by adding tramadol and lornoxicam to prilocaine in IVRA.

Conflicts of interest

The authors declare no conflicts of interest.

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