COMPARISON OF EFFECTS OF TRAMADOL AND KETOROLAC IN INTRAVENOUS REGIONAL ANESTHESIA

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ABSTRACT

Background: Intravenous regional anesthesia, is easy to administer, reliable method for short procedures, however, adjuncts are needed to improve its efficacy. **Objective:** To compare the effects of adding tramodol and ketorolac as adjunct to the lignocaine in intravenous regional anesthesia (IVRA), on intra-operative and postoperative pain. **Material and Method:** A prospective, randomized study was carried out on total of 90 patients who were undergoing upper limb surgery. The patients were divided into three groups as follows: group A received lignocaine 0.5% with tramodol 50 mg, group B was administered lignocaine 0.5% with Ketorolac 30mg, while group C received lignocaine 0.5% only as control. Intra-operatively and post operatively the patient's pain score was evaluated using visual analogue scale (VAS). All the patients were compared for the time to first analgesic. The groups were also compared for the total number of analgesics required in the first twenty-four hours. **Results:** A total of 90 patients were included in this study. The mean age of patients in group A (Lignocaine 0.5% 40ml + Tramadol) was 52±7 years while in group B (Lignocaine 0.5% 40ml + Ketorolac), it was 53±6 years and in Group C (Lignocaine 0.5% 40ml), 50±5 years.Tramadol in lignocaine was found to be significantly better ($p<0.05$) compared to ketorolac in lignocaine and lignocaine alone for intra operative and post operative pain. The patients in tramadol group required significantly less number of analgesics in the first twenty four hours as compared to the other two groups. **Conclusion:** We conclude that as adjunct tramadol is significantly better as compared to ketorolac and lignocaine alone for intravenous regional anesthesia, with respect to operative, post operative analgesia, time to first analgesic and total analgesics in twenty-four hours.

Keywords: Intravenous regional anesthesia, Ketorolac, Tramadol.

INTRODUCTION

Intravenous regional anesthesia (IVRA) was first described in early twentieth century for anesthesia of the hand and forearm.[1] The technique regained popularity in the 1960s when lidocaine was used.[2] Intravenous regional anesthesia is simple to administer, reliable, and cost-effective.[3,4] It is ideal for short operative procedures on the extremities performed on an ambulatory basis. The various disadvantages include local anesthetic (LA) toxicity, slow onset, poor muscle relaxation, tourniquet pain, and minimal postoperative analgesia.[5] The ideal IVRA solution should have the following features: rapid onset, reduced dose, reduced tourniquet pain, and prolonged post-deflation analgesia. At present, this may only be achieved by the addition of adjuncts to LA. Adjuncts used are: opioids (fentanyl, meperidine, morphine, sufentanil), tramadol, non-steroidal anti-inflammatory drugs (ketorolac, tenoxicam, acetyl-salicylate), clonidine, muscle relaxants (atracurium, pancuronium, mivacurium), α2 agonists and neostigmine.[6,7]

Ketorolac, the only NSAID approved for intravenous use interferes with the synthesis of inflammatory mediators.[8] Tramadol is a synthetic opioid analgesic with a unique dual mechanism of action.[9] It exerts agonistic properties at opiate receptors and also interferes with neurotransmitter re-uptake.

This study was designed to compare the effect of adding Tramadol and Ketorolac as adjuncts to lignocaine for IVRA, on intraoperative and postoperative analgesia.

MATERIAL AND METHOD

After approval of the institutional ethical committee and securing informed consent from 90 patients, aged between 20 and 50 years, who were undergoing elective hand or forearm surgery (i.e., carpal tunnel syndrome, trigger finger, and tendon release) or trauma patients were included in this prospective, randomized study. The study was conducted in Department of Anesthesia and Intensive Care, Bahawal Victoria Hospital, Bahawalpur from 1st December 2010 to 30th November, 2011. The patients were randomly allocated to one of the three groups with thirty patients in each group.

Group A: Lignocaine 0.5% 40ml + Tramadol 1ml (50mg).

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Group B: Lignocaine 0.5% 40ml + Ketorolac 1ml (30mg).
Group C: Lignocaine 0.5% 40ml (control).
Randomization was performed using a closed envelope method. Patients with hypersensitivity to local anesthetics, NSAID, or opioids, coagulation disorders, renal dysfunction and sickle cell disease were excluded from the study.
No premedication was given to any patient. After assessing arterial blood pressure, electro-cardiogram, and peripheral oxygen saturation monitoring, two venous cannulae were inserted: one in a vein on the dorsum of the operative hand (20-gauge) and the other in the opposite hand for crystalloid infusion. Exsanguination of the arm of each patient was done with Eschmark's bandage. In case of trauma patient with painful limb, where Eschmark's bandage could not been used, exsanguination was done by elevating the limb above the level of heart for 5 minutes while occluding the brachial artery at cubital fossa. Then, a double-pneumatic tourniquet was applied. The proximal tourniquet was inflated to a pressure of 250 mmHg. Circulatory isolation of the arm was confirmed by inspection, lack of radial pulse, and failure of pulse oximetry tracing of the ipsilateral index finger. After the tourniquet application, patients were injected one of the drug solutions according to the group. After anesthesia was achieved, the distal tourniquet was inflated to 250 mmHg pressure, and the proximal tourniquet was deflated. At the end of surgery, tourniquet deflation was performed using the cyclic deflation technique. The tourniquet was not deflated before 30 minutes even after the surgery was completed and was not inflated for more than 90 minutes.
Intra-operatively, hemodynamic parameters (Arterial blood pressure, heart rate, and peripheral oxygen saturation) and pain was assessed every fifteen minutes, then one hourly for two hours in the recovery room and followed by four hourly in the ward, for the first twenty-four hours. Patients were also monitored for any adverse effects caused by the drugs and the technique. Intra-operatively and postoperatively pain was evaluated using the visual analogue scale (0 = no pain and 10 = worst pain imaginable). If the VAS was more then 5, supplementation was done with sevoflurane in oxygen and nitrous oxide. If the surgery was prolonged, which made it mandatory to release the tourniquet or in case of tourniquet pain, general anesthesia in the form of endotracheal intubation and controlled ventilation with muscle relaxants was used. Intra-operatively no additional analgesics were given. Postoperatively for VAS more than 5, diclofenac sodium 3cc intramuscularly was the rescue drug. Patients were monitored for the time to first analgesic and the total number of analgesic required in the first twenty-four hours. The statistical analysis was performed using SPSS version 16.0. Statistical analysis for comparisons with ANOVA and the 'chi-square' test was done. P value of < 0.05 was considered significant.

RESULTS

A total of 90 patients were included in this study. The mean age of patients in group A (Lignocaine 0.5% 40ml + Tramadol) was 52±7 years while in group B (Lignocaine 0.5% 40ml + Ketorolac), it was 53±6 years and in Group C (Lignocaine 0.5% 40ml), 50±5 years. The mean weight of patients in group A was 68±14 Kg, in group B was 65±10 Kg while it was 72+8 kg in group C. Sex ratio among the study groups was comparable. Group A had 83% male (n=25), 17% female, (n=5); Group B had 80% male (n=24), 20% female (n=6) while the group C had 67% male (n=20), 33% female (n=10).
Heart rate and mean arterial pressure in the three groups of patients is shown in Table I and II respectively. There was no statistical difference between groups when compared for heart rate and mean arterial pressure ($P > 0.05$).There was no incidence of tourniquet pain and also no pain at the surgical site in any patient. Postoperatively the pain score in patients of Group A was significantly better than the pain score of the patients of group B and C ($P<0.05$). Mean visual analogue pain score is shown in Table III. Four patients in group A and B and five patients in group C were converted to general anesthesia because of prolonged surgery and no other side effects were seen.

Table I: Mean values of intra operative heart rate of the study groups.

Time (Minutes)	Group A (n:30)	Group B (n:30)	Group C (n:30)
0	80±7	80±5	81±6
30	81±6	75±5	80±4
60	82±5	70±6	83±6
90	78±6	72±6	78±8

The duration of pain relief in the patients of Group A (16.5±8.2 hours) was significantly better than in the patients of group B and C (p value<0.05) Table IV. The percentage of patients in each group needing an additional analgesic in the first 24 hours is shown in Table IV.

Table II:
Mean values of intra operative mean arterial pressure of the study groups.

Time (minutes)	Group A (n:30)	Group B (n:30)	Group C (n:30)
0 (baseline)	95±10	95±10.5	95±8
30	90±12	80±11.5	90±6
60	95±10.5	75±5.5	85±10
90	100±8	78±5.8	90±8

Table III:
Mean Pain Score (0-10) between the study groups in three groups.

Time	Group A (n:30)	Group B (n:30)	Group C (n:30)
Tourniquet release	1.55±0.55	1.5±0.53	1.5±0.80
01hour after tourniquet release	2.0±0.60	2.0±0.85	2.0±0.90
02 hours after tourniquet release	2.5±0.80	2.5±0.90	3.0±0.25
06 hours after tourniquet relea[se]	2.5±0.85	3.0±0.25	3.25±0.72
10 hours after tourniquet release	2.5±0.80	3.25±0.80	3.50±0.45
14 hours after tourniquet release	3.0±0.25	3.50±0.75	4.0±0.80
18 hours after tourniquet release	3.0±0.30	3.50±0.90	4.0±0.8[2]
24 hours after tourniquet release	3.0±0.55	4.0±0.25	4.25±0.25

(P>0.05)

Table IV:
Time to first analgesia and need of additional analgesics during 1st 24 hrs in three groups.

Group	Group A	Group B	Group C	P. Value
Mean Time to First Analgesic (hours)	16.5±8.2	13.2±7.5	12.5±8.8	<0.05)
Need of additional Analgesics (% of patients)	40 (n=12)	66.6 (n=20)	70 (N=21)	<0.05)

DISCUSSION

The results of our study revealed that the addition of Tramadol or Lignocaine for intravenous regional anesthesia improves the duration of analgesia in the post-operative period. This combination lengthens the time to the first demand of the patient for additional analgesic after surgery.

The injected lignocaine diffuses into the small veins surrounding the nerves and then into the vasa nervorum and capillary plexus of the nerves, leading to conduction block in the nerves involved. It then spreads around the small nerves in the skin, blocking their conduction.[3]

Pain is detected by two different types of peripheral nociceptor neurons: C-fiber nociceptors with slowly conducting unmyelinated axons and A-delta nociceptors with thinly myelinated axons. Surgical trauma results in the release of intracellular contents from damaged cells and from inflammatory cells leading to nociceptors sensitization. The inflammatory mediators from inflammatory cells cause these nociceptors to discharge spontaneously, producing ongoing pain.

NSAID, ketorolac minimizes the activation or sensitization of peripheral nociceptors by anti-inflammatory effects. Unlike other opioids, tramadol causes no respiratory depression and also have no effects on haemodynamics with minimal post operative nausea and vomiting and pruritis and low addiction liability and tolerance. In the past morphine, pethidine and fentanyl have been shown to potentiate Intravenous Regional Anesthesia, but the side effects seen with them make these drugs less popular.[10-12]

Various studies have shown that the addition of tramadol or ketorolac to lignocaine for intravenous regional anesthesia shortens the onset of sensory and motor block, decreases tourniquet pain and improves postoperative analgesia without causing any side effect.[13-15] In our study, there was a significant difference among all three groups for the time to first analgesic in the postoperative period. The onset of analgesia was also rapid in group A as compared to the other groups.

Tramadol 50mg was significantly better as compared to ketorolac 30mg (p<0.05) and lignocaine alone (p<0.05) in the IVRA solution with respect to 24 hours total analgesic requirements. Mean time to first analgesic was also found to be more (p<0.05) in tramadol than other two groups.

We found that, the addition of ketorolac 30mg did not differ from control while tramadol 50mg to IVRA with 0.5% lignocaine has provided an added

advantage of intra operative analgesia, postoperative pain relief and preemptive analgesia without any side effects. Comparing the drugs tramadol and ketorolac, tramadol has shown better pre-emptive analgesic property at the dose of 50 mg compared by reducing the total number of analgesics required in the first twenty-four hours. In our study ketorolac, in the dose used seems to be only marginally beneficial, than lignocaine alone with respect to mean time to first analgesic and 24 hours analgesic requirement ($p>0.05$). The adjuvant drugs (Tramodol and Ketorolac) when added to lignocaine in IVRA were effective in improving the overall quality of anesthesia,[16] and improving the postoperative analgesia in comparison to the control group.

CONCLUSION

We conclude that the addition of tramadol to lignocaine in intravenous regional anesthesia is significantly better than that of ketorolac in lignocaine or use of lignocaine alone, with respect to post operative analgesia, time to first analgesic and total analgesic requirement in the first twenty-four hours after surgery.

REFERENCES

1. Dos Reis A Jr. Intravenous regional anesthesia-first century. Beginning, development, and current status. Rev Bras Anestesiol. 2008;58(3):299-321.
2. Van Zundert A, Helmstädter A, Goerig M, Mortier E. Centennial of intravenous regional anesthesia. Bier's Block. Reg Anesth Pain Med. 2008;33(5):483-9.
3. Blackburn EW, Shafritz AB. Why do Bier blocks work for hand surgery. Most of the time? J Hand Surg Am. 2010;35(6):1022-4.
4. Mohr B. Safety and effectiveness of intravenous regional anesthesia (Bier block) for outpatient management of forearm trauma. CJEM. 2006;8(4):247-50.
5. Vlassakov KV, Bhavani K. The forearm tourniquet Bier block. Logic and authority versus science and experience. Minerva Anestesiol. 2010;76(2):91-2.
6. Rivera JJ, Villecco DJ, Dehner BK, Burkard JF, Osborne LA, Pellegrini JE. The efficacy of ketorolac as an adjunct to the Bier block for controlling postoperative pain following nontraumatic hand and wrist surgery. AANA J. 2008;76(5):341-5.
7. Guay J. Adverse events associated with intravenous Regional anesthesia (Bier block): a systematic review of complications. J Clin Anesth. 2009;21(8):585-94.
8. Suresh S, Wheeler M, Patel A. Case series: IV regional anesthesia with ketorolac and lidocaine: is it effective for the management of complex regional pain syndrome 1 in children and adolescents? Anesth Analg. 2003;96(3):694-5.
9. Siddiqui AK, Mowafi HA, Al-Ghamdi A, Ismail SA, AbuZeid HA. Tramadol as an adjuvant to intravenous regional anesthesia with lignocaine. Saudi Med J. 2008;29(8):1151-5.
10. Ceremuga TE, Gelinas EA, Gonzales JL, Ramos-Alarilla JM. Evaluation of the effects of the addition of morphine sulfate to a standard Bier block solution in peripheral arm surgery. AANA J. 1998;66(5):459-65.
11. Sen H, Kulahci Y, Bicerer E, Ozkan S, Dagli G, Turan A. The analgesic effect of paracetamol when added to lidocaine for intravenous regional anesthesia. Anesth Analg. 2009;109(4):1327-30.
12. McCarthy GC, Megalla SA, Habib AS. Impact of intravenous lidocaine infusion on postoperative analgesia and recovery from surgery: a systematic review of randomized controlled trials. Drugs. 2010;70(9):1149-63.
13. Brill S, Middleton W, Brill G, Fisher A. Bier's block; 100 years old and still going strong! Acta Anaesthesiol Scand. 2004 Jan;48(1):117-22.
14. Alayurt S, Memis D, Pamukcu Z. The addition of sufentanil, tramadol or clonidine to lignocaine for intravenous regional anaesthesia. Anaesth Intensive Care. 2004;32(1):22-7.
15. Ko MJ, Lee JH, Cheong SH, Shin CM, Kim YJ, Choe YK, et al. Comparison of the effects of acetaminophen to ketorolac when added to lidocaine for intravenous regional anesthesia. Korean J Anesthesiol. 2010;58(4):357-61.
16. Choyce A, Peng P. A systematic review of adjuncts for intravenous regional anesthesia for surgical procedures. Can J Anaesth. 2002;49(1):32-45.