Research Article

Comparison of the Effects of Ketorolac to Acetaminophen when addes to Lidocaine for Intravenous Regional Anesthesia

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ABSTRACT

Background and Objective: This study was done to compare the effect of ketorolac and acetaminophen on pain relief during intravenous regional anaesthesia (IVRA).The objective of the study was to evaluate the likely benefits of addition of ketorolac and acetaminophen to lidocaine in intravenous regional anaesthesia in terms of onset and duration of tourniquet pain and also for analgesic requirement in postoperative period.

Method: Hundred patients undergoing hand or forearm surgery received IVRA were assigned in to two groups: Group I received 0.5% lidocaine diluted with 0.9% normal saline plus ketorolac 30 mg made up to a total volume of 40 ml (n = 50), Group II received 0.5% lidocaine diluted with intravenous acetaminophen 300 mg to a total volume of 40 ml (n = 50). Tourniquet pain onset time, which was defined as the time from tourniquet application to Tramadol administration for relieving tourniquet pain and amount of analgesic consumption during surgery were recorded. Following deflation of tourniquet, postoperative pain and quantity of analgesic uses in post-anesthesia care unit were assessed.

Results: Tourniquet pain onset time, postoperative pain and analgesic consumption were same in Group I as compared to Group II ($P < 0.001$).

Conclusions: The addition of ketorolac and acetaminophen to lidocaine for IVRA delays tourniquet pain onset time. Both acetaminophen and ketorolac reduce postoperative pain and analgesic consumption.

Key Words: Ketorolac, Acetaminophen, Lidocaine, Intravenous regional anaesthesia.

INTRODUCTION

Intravenous regional anesthesia (IVRA) was first used by August Bier in 1908[1]. This technique is easy, reliable and cost effective when used in short operative procedures of hand or forearm[2]. Tourniquet pain and lack of postoperative analgesia after tourniquet release are the major limitations to this technique. To improve the efficacy of IVRA, various agents such as tramadol[3], clonidine[4,5], ketamine[6,7], acetaminophen[8-10] and nonsteroidal anti-inflammatory drugs (NSAIDs)[11,12] are added to the local anesthetics, in IVRA.

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Materials and Methods:

Hundred patients with American Society of Anesthegiologists (ASA) physical status I or II, aged between 18 and 50 years, who were scheduled for surgery of the hand or the forearm were included in this study after informed consent. Patients with sickle cell anemia, Raynaud's disease, history of drug allergy, liver and kidney disease were excluded from the study. This prospective, double-blind, interventional study, conducted in the patients undergoing hand or forearm surgery carried out in the operation theater of Orthopedic at Peoples Medical University Hospital from January 2011 to December 2012. Patients were non-randomly divided in two groups: Group I patients received 0.5% lidocaine diluted with 0.9% normal saline plus ketorolac 30 mg made up to a total

volume of 40 ml (n = 50), Group II received 0.5% lidocaine diluted with intravenous acetaminophen 300 mg to a total volume of 40 ml (n = 50). There was no significant difference among groups for age, height, weight, duration of operation time, tourniquet time and sex ratio. No patient was excluded from the study due to technical error. After application of standard monitors, blood pressure (BP), peripheral oxygen saturation (SpO2) and heart rate (HR) were recorded. Two intravenous cannulae were placed, one 20 gauge cannula in the dorsal vein of the operative hand and other 18 gauge in the opposite hand for crystalloid infusion. A double cuff pneumatic tourniquet was applied on the proximal arm of the operative limb. The arm was elevated for 1 minute and exsanguinated. The proximal cuff was inflated to 250 mmHg and arm was lowered. Circulatory isolation of arm was verified by inspection of skin color, absence of radial pulse and loss of pulse oximetry tracing of the ipsilateral index finger. Forty mls of local anaesthetic solution was slowly injected over a period of 60 seconds. After 10 minutes distal cuff was inflated to 250 mmHg, followed by deflation of proximal cuff and surgery was started. Pain was assessed using visual analogue scale (VAS) (0 = no pain and 10 = worst pain imaginable) at 5, 15, 30, 45 and 60 minutes after tourniquet inflation.

Tourniquet was not deflated before 40 minutes and was not left inflated for more than 1 hour. After surgery tourniquet deflation was performed by the cyclic deflation technique. Postoperative pain was further assessed every 30 minutes for 2 hours in recovery room and mean was calculated, using VAS, if found >3, was treated with intravenous tramadol 50mg and total analgesic consumption was recorded. During the intraoperative period and postoperative period, any local or systemic complications were recorded.

Statistical analysis was performed with SPSS version 10. Mean± SD (standard deviation) was computed for demographic data (age, weight), VAS score for intra- and postoperative analgesia and tramadol consumption of both groups. Gender was presented as male to female ratio. The data was analyzed by using 't' test. Significance was assumed at $P < 0.05$.

RESULTS:

The demographic data including age, sex and body weight were comparable in both groups. There was no exclusion from the study because of technical failure. There was also no significant difference in the duration of surgery and tourniquet time. The average age of the patients was 30.45±9.59 years. There were no significant difference between groups for age and weight of the patients. There were 62% male and 38% were female. Most of the patients were ASA-I, 62% and 38% were ASA-II. There was no significant difference between groups when compared intra-operative mean VAS scores as presented in figure 1. Overall intra-operative mean VAS pain score was also not significant between groups (p=0.82) as shown in figure 2. Similarly there was also no significant difference between groups when compared postoperative mean VAS pain score as presented in figure 3. Overall postoperative mean VAS pain score was not significant between groups (p=0.26). Postoperative tramadol requirement was also not significant between groups (26% vs. 30%; p=0.65) as presented in table 1. Average mean tramadol consumption was also similar in both groups (p=0.99) as shown in figure 4.

95% confidence intervals of mean for groups were overlap, which showed intra operative and postoperative mean VAS pain score were not significant between groups after stratification of age, weight and gender. Similarly Postoperative tramadol requirement was also not significant between groups by age, weight and gender. Patients in both the groups remain hemodynamically stable and no patient developed hypotension, hypoxemia, bradycardia or any other adverse events in intraoperative and postoperative period.

DISCUSSION

Orthopedic procedures can cause severe intra-operative and post-operative pain. It is important to achieve optimal post-operative pain control since this will facilitate more rapid achievement of functional outcomes[13]. Intravenous regional anaesthesia (IVRA)[14], is a relatively safe and effective way to provide analgesia for upper extremity surgeries. Limitations to its use include the tourniquet time, tourniquet pain and lack of post-operative analgesia.

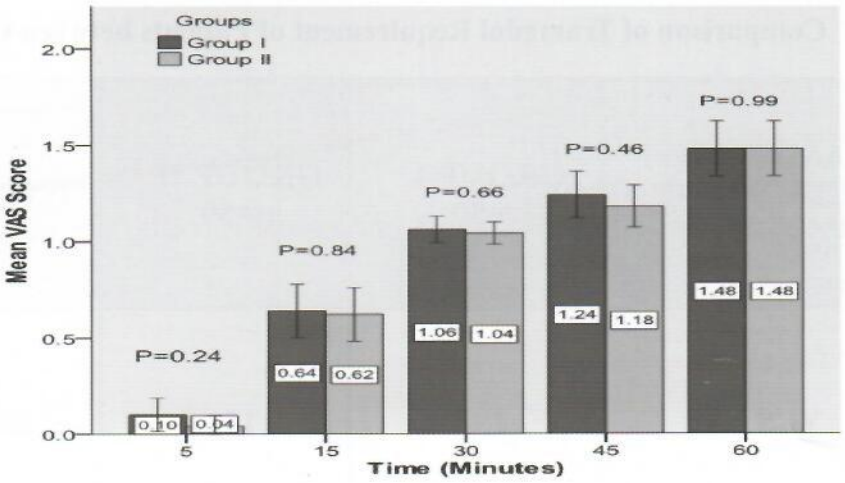


FIGURE-1
Comparison of Intra Operative Vas Pain Score Between Groups With Respect to Time

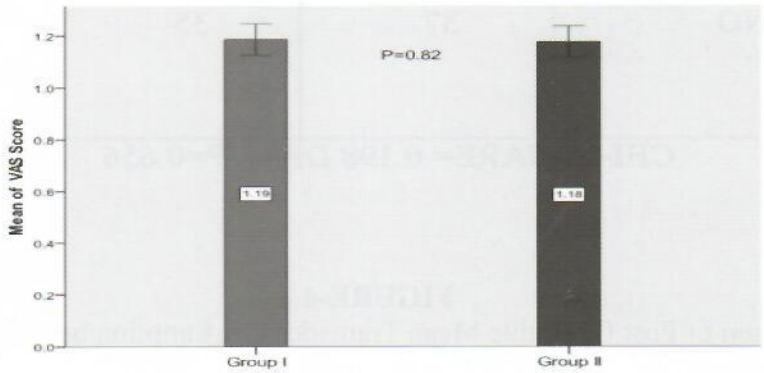


FIGURE-2
Comparison of Overall Intra Operative Mean Vas Pain Score between Groups

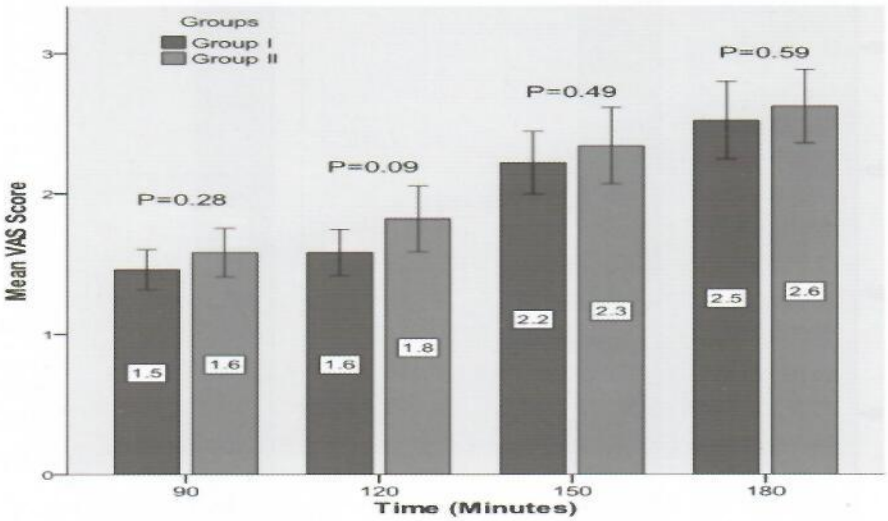


FIGURE-3
Comparison of Postoperative Vas Pain Score between Groups with Respect to Time

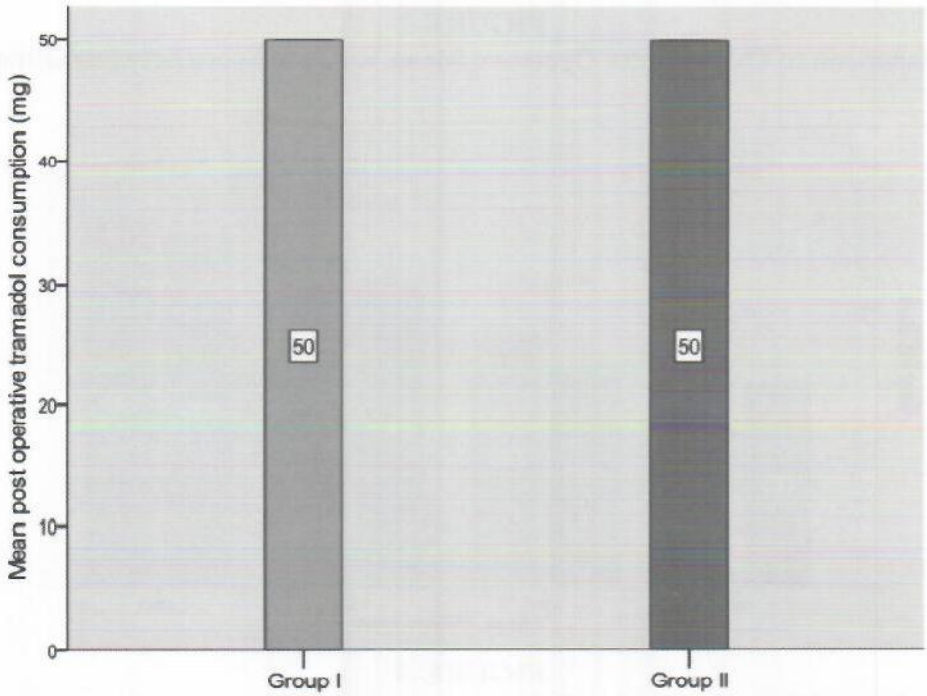
Table-1: Comparison of Tramadol Requirement of Patients between Groups

TRAMADOL REQUIREMENT OF PATIENTS	GROUP I n=50	GROUP II n=50	TOTAL
YES	13	15	28
NO	37	35	72

CHI-SQUARE= 0.198 DF= 1 P=0.656

FIGURE-4

Comparison of Post Operative Mean Tramadol Consumption between Groups



The present study was aimed to evaluate the effects of different drug combinations with lidocaine on intra- and postoperative analgesia by using VAS for pain measurements. In our study we used 40mls lidocaine 0.5% with ketorolac 30mg in group I and 40mls lidocaine 0.5% with acetaminophen 300mg in group II.

Principle outcome of this study was that no significant difference between groups was found when compared intra-operative mean VAS scores. Similarly there was also no significant difference between groups when compared postoperative mean VAS pain score. Average mean tramadol consumption was also similar in both groups. Similarly Postoperative tramadol requirement was also not significant between groups by age, weight and gender. Hence it was proposed to add an analgesic to IVRA, which might reduce both of these problems and act as a modem for pre-emptive analgesia. Ketorolac[15,16] the only NSAID approved for intravenous use interferes with the synthesis of inflammatory mediators. Tramadol[17,18] is a synthetic opioid analgesic with a unique dual mechanism of action. It exerts agonistic properties at opiate receptors and also interferes with neurotransmitter re-uptake.

NSAIDs are widely used concomitantly with IVRA to improve the quality of anesthesia. It is known that the analgesic effect of NSAID is attributed to inhibition of the isoenzyme COX-2 [12] that is primarily associated with inflammation. Cytokines and growth factors enhance the expression and synthesis of COX-2, mainly at inflammatory sites, producing prostaglandins that mediate inflammation, pain and fever. Reuben et al. demonstrated that ketorolac added to lidocaine improved control of tourniquet pain and postoperative pain[19]. Another study suggested that reduction of postoperative pain is as a result of residual ketorolac in the operative arm and its redistribution to the systemic circulation after tourniquet deflation[20]. Studies have indicated that optimal dose of ketorolac for IVRA was 20mg [21], but we used 30mg of ketorolac, as 30mg of ketorolac was shown to be equipotent with 1 g of intravenous acetaminophen[22].

Sen H et al[10], added 300mg acetaminophen to 40ml lidocaine solution for IVRA similar to present study. It improved quality of anesthesia and delayed tourniquet pain onset time, reduced intraoperative and postoperative analgesic consumption. The main mechanism of analgesic effect of acetaminophen is demonstrated to be through its action on central nervous system mediated by inhibition of prostaglandin synthesis[23,24]. Acetaminophen is also shown to inhibit cyclooxygenase (COX) enzyme in vivo[25,26]. Several studies have demonstrated the peripheral antinociceptive effect of acetaminophen.

In Myoung et al[27] study, postoperative pain and postoperative analgesic consumption were decreased in Ketorolac with lidocaine than only lidocaine but were ineffective in decreasing tourniquet pain and onset time of sensory block. Ketorolac 10mg when added to IVRA may be insufficient to reduce tourniquet pain but its anti-inflammatory effect and systemic circulation after tourniquet deflation may reduce postoperative pain.

Lee et al[28]. have suggested that acetaminophen selectively suppressed peripheral prostaglandin E2 release and increased COX-2 gene expression in a clinical model of acute inflammation. In another study, acetaminophen may also interfere with the delivery of peripheral ß-endorphins and help in reducing the pain[29]. Jamil et al[11]. Studied that the quality of analgesia was excellent when ketorolac was added to lignocaine for IVRA. Degree of block and duration of postoperative analgesia both were better in patients with ketorolac and lignocaine than in patients with lignocaine alone. Canbay et al[30]. Studied that 50mg of intravenous acetaminophen pretreatment is effective in reducing the pain on propofol injection. Dani et al[31]. Suggested that paracetamol exhibits local antinociceptive effects by modulating cannabinoid receptors. Vanos et al[32], found that IVRA block containing ketorolac was successful and that the combination with lidocaine provided short-term additional analgesia, allowing the patients to undergo physical therapy.

Hord et al [33], who combined lidocaine with bretylium, found that the lidocaine IVRA blocks produced a mean pain relief of 2.7 days, whereas the combination with bretylium produced a mean relief of 20.0 days.

McKain et al[34] found that lidocaine IVRA failed to produce pain relief beyond the duration of the block. There is thus a general consensus that

IVRA blocks that only contain lidocaine will provide short-term relief and that the mixture of two drugs is necessary for prolonged relief. The precise cellular mechanism responsible for the alteration in peripheral nociceptor sensitivity following tissue trauma are not known[35]. Chemical mediators such as prostaglandins are believed to modify nociceptor input leading to mechanical allodynia. The only symptom that was predictive of failure with IVRA lidocaine and ketorolac was allodynia.

Yousad et al[36] Ketorolac added to Lidocaine in IVRA increases degree of anaesthesia and also provide prolonged postoperative analgesia.

CONCLUSION:

In conclusion, the addition of intravenous acetaminophen or ketorolac to lidocaine in IVRA improves tourniquet pain, prolong the time to first analgesic requirement and decrease the total amount of analgesic, without side effects.

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