Melatonin Versus Ketorolac as an Adjuvant in Lidocaine Intravenous Regional Anesthesia

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Abstract

Background and Objectives: Melatonin and Ketorolac delay and minimize intraoperative tourniquet pain when used as premedication to lidocaine-based intravenous regional anesthesia (IVRA). It is unclear if Melatonin is more efficacious compared with Ketorolac. This study compared intraoperative tourniquet pain, postoperative analgesia, and side effects of using Melatonin vs. Ketorolac during outpatient hand surgery.

Methods: A total of 78 patients scheduled for hand and forearm surgery were randomly assigned to one of three groups; the control group (Patients received 3mg/kg Lidocaine made with 40ml normal saline), Melatonin group (Patients received 3mg/kg Lidocaine made with 40ml normal saline plus oral Melatonin 0.15mg/kg one hour preoperatively) and Ketorolac group (Patients received 3mg/kg Lidocaine made with 40ml normal saline with an adjuvant Ketorolac 20mg). Ten minutes after proximal tourniquet inflation, the distal tourniquet was inflated, and the proximal tourniquet deflated. Tourniquet pain was measured every 10mins. Need for intraoperative opioids were recorded, PACU pain scores, postoperative analgesic consumption, patients and surgeon satisfaction were compared. Patients were contacted 24hrs after surgery and reported their analgesic consumption, satisfaction scores.

Results: Hemodynamic stability was recorded among patients of the three groups. Intra-operative pain score was significantly lower while the time of first request of analgesia was significantly longer in the Melatonin and Ketorolac groups than the control group. 24h postoperative analgesic consumption was higher in the Melatonin and the control group than Ketorolac group. Patients and Surgeon satisfaction were significantly higher with Melatonin and Ketorolac than in the control group.

Conclusion: Both Melatonin and Ketorolac are effective adjuvant to Lidocaine during intravenous regional anesthesia with hemodynamic stability. However Ketorolac is characterized by being more effective in terms of postoperative analgesia as denoted by time of first request of analgesia and total dose of analgesia given.

Key Words: Intravenous regional anesthesia (IVRA) – Melatonin – Ketorolac.

Introduction

THE Bier block has multiple advantages, including ease of administration, rapidity of recovery, rapid onset, muscular relaxation, and controllable extent of anesthesia. It is an excellent technique for short (<90 minutes) open surgical procedures and for closed reductions of bony fractures [1]. Three limitations of IVRA can be defined “traditional”: relatively slow onset time, tourniquet pain, lack of postoperative analgesia [2]. The ideal IVRA solution should have the following features: Rapid onset, reduced dose of local anesthesia (LA), reduced tourniquet pain, and prolonged post deflation analgesia [3]. At present, this is achieved by the addition of adjuncts, including opioids, tramadol, nonsteroidal anti-inflammatory drugs (ketorolac, acetylsalicylate, parecoxib, lornoxicam), dexmedetomidine, clonidine, dexamethasone, butorphanol, muscle relaxants Atracurium, neostigmine, ketamine and magnesium, alkalinization with sodium bicarbonate, potassium and temperature of LA. Lately, nitroglycerin and dexamethasone have also been tried. Premedication with gabapentine and melatonin to improve the quality of IVRA has also been described [4,5].

The aim of the work is to compare the efficacy of melatonin versus ketorolac as adjuvants to Lidocaine during Intravenous Regional Anesthesia, with regard to tourniquet pain, quality of anesthesia and peri-operative analgesia.

Material and Methods

This study was a randomized controlled clinical trial done at the Suez Canal University Hospital in the routine and emergency surgical theaters between June 2011 and August 2012. Inclusion criteria; patients undergoing elective, emergency hand or forearm surgeries, age between 18-60
years, both sexes and ASA I or II. Exclusion criteria: sickle cell disease, Raynaud’s disease, scleroderma, allergy to local anesthetics, Severe hypertensive or peripheral vascular disease, local infection, skeletal muscle disorders or Paget’s disease (local anesthetic may spread to the systemic circulation via venous channels in the bone), history of fits and cardiac arrhythmia. The detectable difference between the means of the group using the time before the first request for analgesia & it equals 273min. The calculated sample was 24/group. 10% is considered as drop out rate so the final sample size was 26 in each group, (total 78 subjects). Seventy eight patients were divided randomly into three groups. Group 1 (Control group): (26 patients), IVRA was done using 3mg/kg Lidocaine made with 40ml normal saline. Group 2 (melatonin group): (26 patients), IVRA was done using 3mg/kg. Lidocaine made with 40ml normal saline with an adjuvant oral melatonin 0.15mg/kg Melatonin®: Manufactured by Nature’s Bounty, INC. Bohemia, New York. 11716 USA. Supplement Facts: Serving size 1 tablet, amount per serving Melatonin 3mg (as n-Acetyl-5-Methoxytryptamine) one hour preoperatively. Group 3 (Ketorolac group): (26 patients), IVRA was done using 3mg/kg Lidocaine made with 40ml with normal saline an adjuvant IV ketorolac 20mg. Patients were fasting for at least 6-8 hours, airway devices, anesthesia machine and equipments were checked promptly. Monitoring equipments (Datex-OhmedaTM) were attached to the patient including 3 leads ECG, non-invasive blood pressure and pulse oximetry. All patients were pre-medicated using Midazolam 0.1mg/kg IV given 30min before surgery. Patients were asked to be in the supine position with the arm to be blocked elevated to achieve passive exsanguination.

The double tourniquet was applied on the arm with generous layers of padding. Two IV cannulae were placed, one in a vein on the dorsum of the operative hand for the IVRA, and the second in the opposite hand for administering supplemental medications and fluids during the operation. After a pneumatic double tourniquet had been placed around the upper arm, the extremity was elevated. The proximal cuff was then inflated 100mm Hg above the systolic blood pressure and the circulatory isolation of the arm was verified by inspection, absence of radial pulse, and loss of the pulse oximetry tracing in the ipsilateral index finger. The extremity was then lowered and the local anesthetic was slowly injected through the previously inserted IV catheter. Ten minutes later, the distal tourniquet was inflated, which overlies part of the anesthetized arm and then the proximal one was deflated, at the end of surgery, the cuff was not deflated until 20 minutes after local anesthetic injection, cuff deflation was performed in cycles with deflation/inflation times of less than 10 seconds, and The patient was monitored closely for 20 minutes following tourniquet release.

Haemodynamic parameters (pulse, blood pressure and respiratory rate) were recorded before inflation of the tourniquet (base line), after inflation of the tourniquet, immediately after drug injection, every 5 minutes after drug injection for 30 minutes, immediately after deflation of the tourniquet, every 5 minutes after deflation of the tourniquet for 20 minutes, Just before the transfer of the patient to the recovery room. Onset, recovery and duration of sensory and motor blockade, the duration of surgery (from skin incision time to skin closure time), the quality and efficacy of the block were assessed by intraoperative tourniquet pain using Visual Analogue Score. Patient satisfaction: Excellent, good, fair or poor and Surgeon satisfaction: Excellent, good, fair or poor. Time of the first request of analgesia and total analgesic consumption in the first post-operative 24 hours were calculated. The initial time of tourniquet pain, defined as the time elapsed between the distal cuff inflation and the patient’s initial complaint of tourniquet pain, was recorded. Intraoperative and postoperative rescue analgesia was provided with Morphine 2 mg boluses whenever the patient complained of pain with VAS >3. Complications were recorded, as dizziness, nausea, vomiting, tinnitus, perioral tingling, hypotension, muscle twitching, loss of consciousness, and convulsions.

Statistical analysis:

Data entry and analysis by using the “SPSS 10.0” for Windows program with the aid of the following statistical tests; Continuous Variables were presented as means±SD. Discrete variables were expressed as frequencies and percentages. Differences between the three groups using students t-test for continuous variables [6].

Chi-square for discrete variable differences were statistically significant if the probability (p 0.05). Presentation of the statistical outcomes and tables was performed using the “Microsoft Word 2003” program.

Results

All of the three groups of the study were matched as regards age, sex, patients’ weight and ASA status of the patients. There was no statistically
significant difference between the three groups of the study as regards the duration of the operation and type of the surgery (Tables 1,2).

Hemodynamic stability was recorded among patients of the three groups as no significant difference between the three groups regarding heart rate, systolic blood pressure and diastolic blood pressure throughout the period of the operation till the transfer of the patient to the recovery room.

Intra-operative pain score was significantly lower in the melatonin and ketorolac groups than the control group (20-60 minutes) with p-value ranging from (0.02 to <0.001). No significant difference was estimated between both melatonin and ketorolac groups (Table 3).

The time of first request of analgesia was significantly longer in both melatonin and ketorolac groups than the control group (p<0.001) Patients received ketorolac had requested their first dose of analgesia after significantly longer time than patients received melatonin (735.6 versus 196.5 minutes) (Table 4).

The total dose of analgesia given to patients in 24 hours in the control group was significantly higher than doses given to patients in melatonin and ketorolac groups (Fig. 1).

Assessment of patient satisfaction was significantly higher with melatonin and ketorolac than in the control group. No significant difference was reported between both melatonin and ketorolac groups. Surgeon satisfaction was significantly higher with melatonin and ketorolac than in the control group (Tables 5,6).

Table (1): Demographic characteristics and ASA status of the patients.

<table>
<thead>
<tr>
<th></th>
<th>Control Gr. (n=26)</th>
<th>Melatonin Gr. (n=26)</th>
<th>Ketorolac Gr. (n=26)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>31.4±11.6</td>
<td>28.6±9.1</td>
<td>29.5±12.6</td>
<td>0.6 (NS)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>19 (73.1%)</td>
<td>20 (76.9%)</td>
<td>18 (69.2%)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>7 (26.9%)</td>
<td>6 (23.1%)</td>
<td>8 (30.8%)</td>
<td>0.8 (NS)</td>
</tr>
<tr>
<td>ASA</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ASA I</td>
<td>20 (76.9%)</td>
<td>17 (65.4%)</td>
<td>16 (61.5%)</td>
<td>0.5 (NS)</td>
</tr>
<tr>
<td>ASA II</td>
<td>6 (23.1%)</td>
<td>9 (34.6%)</td>
<td>10 (38.5%)</td>
<td></td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>70.5±6.1</td>
<td>72.4±7.3</td>
<td>71.5±10.5</td>
<td>0.7 (NS)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>64.79</td>
<td>63.81</td>
<td>65.83</td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration of surgery (min)</td>
<td>36.1±7.8</td>
<td>38.3±6.7</td>
<td>35.4±8.1</td>
<td>0.4 (NS)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>(25-45)</td>
<td>(30-55)</td>
<td>(25-50)</td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Data are expressed as means (SD (range)) and number (%).
NS: No statistically significant difference (p-value >0.05).

Table (2): Type of surgery.

<table>
<thead>
<tr>
<th>Type of surgery</th>
<th>Control Gr. (n=26)</th>
<th>Melatonin Gr. (n=26)</th>
<th>Ketorolac Gr. (n=26)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ganglion excision</td>
<td>6 (23.1%)</td>
<td>7 (26.9%)</td>
<td>6 (23.1%)</td>
<td></td>
</tr>
<tr>
<td>Tendon repair</td>
<td>7 (26.9%)</td>
<td>5 (19.2%)</td>
<td>6 (23.1%)</td>
<td></td>
</tr>
<tr>
<td>Carpal tunnel release</td>
<td>6 (23.1%)</td>
<td>5 (19.2%)</td>
<td>7 (26.9%)</td>
<td>0.9 (NS)</td>
</tr>
<tr>
<td>Trigger finger release</td>
<td>3 (11.5%)</td>
<td>2 (7.7%)</td>
<td>3 (11.5%)</td>
<td></td>
</tr>
<tr>
<td>Fracture ulna</td>
<td>2 (7.7%)</td>
<td>3 (11.5%)</td>
<td>2 (7.7%)</td>
<td></td>
</tr>
<tr>
<td>Both forearm bone fracture</td>
<td>2 (7.7%)</td>
<td>4 (15.4%)</td>
<td>2 (7.7%)</td>
<td></td>
</tr>
</tbody>
</table>

NS: No statistically significant difference (p-value >0.05).
Table (3): Intra-operative degree of tourniquet pain by using the Visual Analogue Scale (0-10 VAS).

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Control Gr. (n=26)</th>
<th>Melatonin Gr. (n=26)</th>
<th>Ketorolac Gr. (n=26)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 minutes</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>–</td>
</tr>
<tr>
<td>20 minutes</td>
<td>2 (0-3)</td>
<td>0#</td>
<td>0#</td>
<td>0.02*</td>
</tr>
<tr>
<td>30 minutes</td>
<td>2 (1-3)</td>
<td>1 (0-2)#</td>
<td>1 (0-1)#</td>
<td>0.01*</td>
</tr>
<tr>
<td>40 minutes</td>
<td>3 (1-4)</td>
<td>1 (0-2)#</td>
<td>1 (0-1)#</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>50 minutes</td>
<td>3 (2-4)</td>
<td>1 (0-2)#</td>
<td>1 (0-1)#</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>60 minutes</td>
<td>4 (2-5)</td>
<td>1 (0-2)#</td>
<td>1 (0-2)#</td>
<td>&lt;0.001*</td>
</tr>
</tbody>
</table>

Data are expressed as median (range).
* : Statistically significant difference (p-value of ANOVA test).
# : Statistically significant difference versus control group (post hoc analysis using the Bonferroni test).

Table (4): Time of first request of analgesia (morphine).

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Control Gr. (n=26)</th>
<th>Melatonin Gr. (n=26)</th>
<th>Ketorolac Gr. (n=26)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (SD)</td>
<td>31.5±10.6</td>
<td>196.5±54.9#</td>
<td>735.6±94.8#</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Range</td>
<td>(10-60)</td>
<td>(110-230)</td>
<td>(540-840)</td>
<td></td>
</tr>
</tbody>
</table>

Data are expressed as means [SD (range)].
* : Statistically significant difference (p-value of ANOVA test).
# : Statistically significant difference versus control group (post hoc analysis using the Bonferroni test).

Table (5): Patient satisfaction.

<table>
<thead>
<tr>
<th>Patient satisfaction</th>
<th>Control Gr. (n=26)</th>
<th>Melatonin Gr. (n=26)</th>
<th>Ketorolac Gr. (n=26)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Excellent</td>
<td>3 (11.5%)</td>
<td>18 (69.2%)*</td>
<td>20 (76.9%)*</td>
</tr>
<tr>
<td>Good</td>
<td>10 (38.5%)</td>
<td>7 (26.9%)</td>
<td>6 (23.1%)</td>
</tr>
<tr>
<td>Fair</td>
<td>11 (42.3%)</td>
<td>1 (3.9%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Poor</td>
<td>2 (7.7%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

Data are expressed as numbers (%).
* : Statistically significant difference versus control group.

Table (6): Surgeon satisfaction.

<table>
<thead>
<tr>
<th>Surgeon satisfaction</th>
<th>Control Gr. (n=26)</th>
<th>Melatonin Gr. (n=26)</th>
<th>Ketorolac Gr. (n=26)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Excellent</td>
<td>8 (30.8%)</td>
<td>21 (80.8%)*</td>
<td>24 (92.3%)*</td>
</tr>
<tr>
<td>Good</td>
<td>14 (53.8%)</td>
<td>5 (19.2%)</td>
<td>2 (7.7%)</td>
</tr>
<tr>
<td>Fair</td>
<td>4 (15.4%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Poor</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

Data are expressed as numbers (%).
* : Statistically significant difference versus control group.

Table (7): Incidence of complications.

<table>
<thead>
<tr>
<th>Complications</th>
<th>Control Gr. (n=26)</th>
<th>Melatonin Gr. (n=26)</th>
<th>Ketorolac Gr. (n=26)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>23 (88.5%)</td>
<td>24 (92.3%)</td>
<td>24 (92.3%)</td>
<td>0.8</td>
</tr>
<tr>
<td>Dizziness</td>
<td>3 (11.5%)</td>
<td>2 (7.7%)</td>
<td>2 (7.7%)</td>
<td>(NS)</td>
</tr>
</tbody>
</table>

NS: Not statistically significant difference (p-value >0.05).

Fig. (1): Total given dose of analgesia during first 24 hours.
* : Statistically significant lower in melatonin and ketorolac versus control group.
# : Statistically significant difference between melatonin and ketorolac group.
‡: Statistically significant difference between melatonin and ketorolac group (post hoc analysis using the Bonferroni test).

Discussion

The inability to provide effective postoperative analgesia is one of the major disadvantages of IVRA [7]. A large number of adjuvants like NSAIDs, opioids, a2 agonists, muscle relaxants, NMDA agonist (as ketamine) had been added to local anesthetic to reduce tourniquet pain and thereby increase tourniquet tolerance and enhance postoperative analgesia [8].

Control of postoperative pain is a very important factor in evaluating an adjuvant to anesthetic in IVRA. The main findings in this study were that 0.15mg/kg oral melatonin and I V 20mg ketorolac added to lidocaine IVRA was effective in decreasing tourniquet related pain, and enhanced intraoperative and postoperative analgesia without producing clinically significant side effects, but ketorolac was more effective in postoperative pain control at the time of first request of analgesia was prolonged and total dose during the first 24 hours was decreased.

In the present study, all groups were matched for age, sex, ASA status and weight. Hemodynamic
stability was noted among all patients in the three groups throughout the duration of the surgery after tourniquet inflation and also after tourniquet deflation. Neither drugs used nor technique had perioperative hemodynamic instability. In the study by Ismail and Mowafi, the 10-mg oral dose of melatonin produced significant and prolonged reductions in mean arterial blood pressure [9]. In a randomized, double-blind study, prolonged administration of melatonin (a 3-week course of a daily slow-release 3-mg melatonin pill) did not influence diurnal blood pressure but did significantly decrease nocturnal blood pressure without modifying heart rate in women [10]. The hemodynamic effects of oral melatonin in different doses and age groups need to be further studied.

Intra-operative pain score was significantly lower in the melatonin and ketorolac groups than the control group (10-60 minutes). No significant difference was estimated between both melatonin and ketorolac groups.

Perioperatively, melatonin has been used as a premedicant, sedative and analgesic. It decreases Paediatric emergence delirium. The antioxidant properties of melatonin are being investigated for use in sepsis and reperfusion injuries [11].

A qualitative systematic review of the literature concerning the perioperative use of melatonin as an anxiolytic or analgesic in adult patients was carried out using the recommended guidelines provided by the Cochrane Handbook for Systematic Reviews of Interventions. Nine of the 10 studies showed statistically significant reduction of preoperative anxiety with melatonin premedication compared with placebo. An opioid-sparing effect or reduced pain scores were evident in five studies, whereas three studies were contradictory [11].

Melatonin improves tourniquet tolerance and enhances postoperative analgesia in patients receiving intravenous regional anesthesia (IVRA). Melatonin is an effective premedication before IVRA since it reduced patient anxiety, decreased tourniquet-related pain, and improved perioperative analgesia [12].

Ismail et al., stated that premedication with 10mg oral melatonin provided amelioration, enhanced perioperative analgesia, decreased the intracocular pressure (IOP), and improved the operating conditions during cataract surgery under topical anesthesia [9]. Number of previous studies (13-15) have reported a significantly lower pain scores in the melatonin group compared with the control group. In a clinical study, it was found that a pre-emptive oral dose of 6mg of melatonin reduced the pain scores and pethidine requirements in the first post-operative 24 hours in patients undergoing abdominal surgery [13].

Two further studies [14,15]. Pre-operative oral melatonin 6mg, the night before and 1 hour before surgery, decreased pain scores and tramadol consumption and enhanced sleep quality and sedation scores during the post-operative period in patients undergoing elective prostatectomy. The second study Caumo et al., investigated ASA I/II patients (n=59), who were randomized to receive either oral melatonin (5mg), oral clonidine (100µg) or placebo both the night before and one hour prior to anesthesia. The melatonin and clonidine groups had lower anxiety scores, lower pain scores and lower morphine consumption in the first 24 hours postoperatively. However, subgroup analysis indicated that the decrease in pain scores and morphine consumption was only significant in those patients with higher preoperative anxiety scores. It was declared that the co-administration of melatonin and clonidine as a preoperative premedication decreased the postoperative morphine use by more than 30% in patients undergoing abdominal hysterectomy with moderate and severe anxiety, whereas in mildly anxious patients, it was not associated with an analgesic effect. The benefits of these interventions were statistically and clinically significant to produce postoperative anxiolysis, which led to lower postoperative pain, as well as lower morphine consumption throughout the first 24 hours after surgery.

Anxiolytic and analgesic effects of melatonin may improve the control of post-operative pain by controlling the higher anxiety that accompanies surgical interventions. The hypnotic, anti-nociceptive and anticonvulsant properties of melatonin created a profile of a novel hypnotic anesthetic agent. The similarity between the results of these studies and our study may be due to anxiolysis by midazolam premedication, balanced anesthesia technique and the shorter duration of surgery.

Ketorolac added to IVRA at a dose up to 20mg reduced tourniquet pain, but the potential of ketorolac in causing a wound hematoma by localized platelet inhibition had not yet been examined by any published Study [16]. As regards the time of first request of analgesia in the three groups of the present study, patients in both melatonin and ketorolac groups showed significantly longer postoperative time before first request of analgesia. When comparing melatonin to ketorolac we had found that patients received ketorolac had requested their first dose of analgesia after significantly longer time than patients received melatonin (735.6 versus...
196.5 minutes). We had estimated that total dose of morphine given to patients in 24 hours. In the control group, this dose was significantly higher (12.1mg) than doses given to patients in melatonin (6.9mg) and ketorolac groups (4.6mg).

In the present study, both surgeon and patient satisfaction have been evaluated. Patient satisfaction was significantly higher with melatonin and ketorolac than in the control group. No significant difference was reported between both melatonin and ketorolac groups. Surgeon satisfaction was significantly higher with melatonin and ketorolac than in the control group. No significant difference was reported between both melatonin and ketorolac groups.

Lidocaine IVRA is safe and effective. Release of the tourniquet 5 minutes after the administration of 2.5mg/kg of 0.5% lidocaine resulted in no signs of cardiovascular or CNS toxicity; however, symptoms of tinnitus were noted between 20 and 70 seconds after deflation [17,18]. Tucker and Boas, showed that approximately 70% of lidocaine remains within the tissues of the previously isolated limb following tourniquet release, the remainder entering the general circulation in the subsequent 45 minutes [18]. In the present study, the only reported complication among the studied patients in the three groups of the study was dizziness with no statistically significant difference. Reuben and co-workers had evaluated the efficacy of adjuvant Ketorolac to Lidocaine in IVRA among sixty patients subjected to elective hand surgery. They showed that patients received ketorolac reported significantly less intra-operative tourniquet pain with lower verbal analog pain scores at 15 and 30 minutes after tourniquet inflation than estimated among the control group [16]. These results are consistent with our study. They also showed that ketorolac 60mg added to IVRA might give up to 12-16 hours of postoperative analgesia which is consistent with our study. The same group later reported in a dose ranging study using an upper arm tourniquet that the benefits of ketorolac incrementally increase up to 20mg and no further benefits are evident with larger doses [19].

Reuben and co-workers, also had found that patients received ketorolac required fewer analgesic tablets (Tylenol No 3 “acetaminophen 325mg/codeine 30mg”) compared to control group [16]. These results are consistent with our study. Possibly, those derived from residual ketorolac in the operative arm, although some redistribution of ketorolac to the systemic circulation would be expected to occur after tourniquet deflation, possibly producing some late analgesia.

Sunita and colleagues [20], compared between Ketorolac and Tramadol as adjuvants to lidocaine in IVRA, among sixty ASA class I & II patients undergoing either elective or emergency upper extremity surgery. They reported that 30% patients in each saline and ketorolac group required general anesthesia (GA) supplementation for tourniquet pain ($p >0.05$). These results are inconsistent with our study. This could be explained by inefficient exsanguination. As all these patients had painful limb and exsanguination was done by raising the limb above the heart level for 5 minutes without compression of the artery. This perhaps led to dilution of the IVRA drug, which resulted in inadequate analgesia and hence tourniquet pain intra-operatively.

In the study done by Bose et al., [8] among sixty ASA I & II aged 16 to 60 years undergoing elective hand or forearm surgeries to compare between ketamine and ketorolac as adjuvants to lidocaine in IVRA, they have found that the intra-operative visual analogue scale (VAS) scores were significantly lower in ketamine and ketorolac groups for 40-60min. and 40-90min. respectively in comparison to control group. These results are consistent with our study, but in our study, the evaluation of intra-operative degree of tourniquet pain in the three groups of the study was only for 60 minutes and this was limited by the duration of surgery in the studied groups.

Regarding time to request for first rescue analgesia (fentanyl), Bose et al., [8] found that it was significantly shorter in the control group than adjuvant groups (ketamine and ketorolac). They reported that postoperative analgesia consumption (fentanyl) was significantly higher in the control group in comparison to Ketamine and ketorolac which is consistent with our findings. They were also concerned with patient satisfaction with the adjuvant and had shown similar results to ours. They have reported that patients’ satisfaction scores were significantly better in the adjuvant groups (Ketamine and ketorolac) in comparison to control group.

Jankovic et al., [21] evaluate the analgesic effectiveness of ketorolac and Dexamethasone when added to lidocaine for IVRA among forty-five ASA physical status I-II patients. They found that the intra-operative visual analogue scale (VAS) scores were significantly lower in the ketorolac group at 15, 30, 45 and 60 minutes after tourniquet inflation in comparison to control group. These results are consistent with our study. Also and Similar to our study, they found that patients in the ketorolac
group had significantly longer period of subjective comfort during which they required no analgesics, with a median of 524min (range: 415-1085min) compared with 122min (range: 34-392min) for the control group. They also reported that two of the 15 patients of ketorolac group required no additional analgesics (ketorolac tablets) during the first 24 hours after tourniquet release while all patients in the control group required ketorolac tablets. Also, they found that the total ketorolac tablet consumption during the first 24 hours after surgery was less in the ketorolac group compared to control group. Their results were consistent with ours in terms of control postoperative pain when compared to control group.

References