Intraarticular Ketamine Extended the Duration of Lidocaine Analgesia. A Comparative Study with Bupivacaine in Patients Undergoing Knee Arthroscopic Surgeries

TAREK M. EL-MENESY, M.D.*; GHADA A. HAMDEN, M.D.**; AHMAD A. BADWAY, M.D.** and NAHLA A. EL-KADY, M.D.**

From Department of Anesthesia, Faculties of Medicine, Beni Suef * and Cairo** Universities.

Abstract

Background: The duration of lidocaine analgesia is shorter than that of bupivacaine. This study was designed to evaluate the efficacy of ketamine in extending the duration of intraarticular lidocaine 1% analgesia to reach that of bupivacaine 0.25%. Also, to evaluate the pain scores, tramadol consumption and the associated side effects.

Methods: This randomized double-blind study was conducted on sixty patients ASA I and II and undergoing arthroscopic knee surgeries. The patients were allocated into 3 groups: ketamine-lidocaine group: where ketamine 1mg/kg was added to 20ml of intraarticular lidocaine 1%; lidocaine group: where 20ml of intraarticular lidocaine 1% was given and bupivacaine group: where 20ml of bupivacaine 0.25% was given. The duration of postoperative analgesia, the pain scores and total analgesic consumption in 24 hours were compared. Also, the hemodynamics and the occurrence of side effects were reported.

Results: The duration of analgesia was prolonged and the pain scores at 4 hour were reduced in ketamine-lidocaine and bupivacaine treated groups when compared to lidocaine only group. However, no significant difference was detected between the groups as regards tramadol requirements in the 24 hours of the study period. The occurrence of vomiting was comparable between the studied groups.

Conclusion: When ketamine 1mg/kg was added to intraarticular 20ml of lidocaine 1% it prolongs its duration to reach that of bupivacaine 0.25% in the same volume without significant side effects. However, the total analgesic needs in 24 hours were similar in the three studied groups.

Key Words: Ketamine – Lidocaine – Bupivacaine – Analgesia – Tramadol consumption.

Introduction

EFFECTIVE postoperative pain relief following diagnostic and therapeutic arthroscopic knee surgery is an important issue that permit early discharge and improve comfort and mobility at home [1]. Intraarticular local anesthetic injection is often used for the management and prevention of such pain [2]. The intraarticular injection not only reduces postoperative pain but it can provide efficient intraoperative anesthesia which may help to accomplish arthroscopic knee surgery [3] and shoulder manipulation [4]. Although bupivacaine was believed to be the local anesthetic of choice for such type of procedures and was used with and without adjuvants in previous reports but still other local anesthetics are tested and used in an effective manner [5,6]. When administered in regional blocks, lidocaine was believed to be shorter in duration than bupivacaine and furthermore when added to bupivacaine it results in reduction of its duration of analgesia [7]. Ketamine is NMDA receptor antagonist which plays an important role in calcium channel blockage and therefore pain control as the calcium is responsible for pain transmission [8]. In addition to that, ketamine was believed to have local anesthetic like action due to its block effect on sodium channels similar to lidocaine and bupivacaine [9]. Also, Zhang and his colleagues [10] proved that the peripheral administration of NMDA receptor antagonists; ketamine and memantine in rats has a prophylactic analgesic effects in arthritic pain due to the decrease in central nociceptive inputs which can be applied in humans. In a recent study, Ayoglu and his colleagues [11] demonstrated that intraarticular use of ketamine improved the postoperative analgesia produced by tramadol.

This study was directed to find out if the combined use of intraarticular ketamine 1mg/kg together with lidocaine 1% may prolong lidocaine duration of analgesia to the extent that it may reach the duration of bupivacaine 0.25% alone. The study also searched for its effect on pain scores and analgesic requirements and whether it is associated with systemic side effects.
Patients and Methods

This study was conducted on 60 patients, ASA physical status I & II and undergoing therapeutic knee arthroscopic surgeries (ACL anterior cruciate ligament reconstruction and meniscectomy) following agreement by local ethical committee and obtaining informed consents from patients included in this study. The study was conducted in Dar Al Shifa hospital in the period between July 2007 to November 2008.

Patients were excluded from this study if was presented with ASA physical status >2, any mental or neurological disorders that affect pain assessment, having a history of analgesic intake within the previous 24 hours or known to have hypersensitivity to lidocaine or bupivacaine.

Before premedication, patients were taught about the visual analogue scale (VAS) for evaluation of postoperative pain.

Forty five minutes prior to surgery, the patients received oral midazolam 5mg. General anesthesia was induced with fentanyl 2 µg/kg and propofol 2.5mg/kg followed by cisatracurium 0.15mg/kg to facilitate orotracheal intubation. Intraoperatively, the patients were monitored by electrocardiogram, pulse oximetry, noninvasive blood pressure and capnography. Anesthesia was maintained by isoflurane 1% in 50%: 50% O₂/N₂O mixture and ventilation was adjusted to maintain normocapnea (ETCO₂ between 35 and 40mmHg). Intraoperative muscle relaxation was achieved by incremental doses of cisatracurium every 25 minutes.

At the end of the procedure, the intraarticular cavity was sealed by suturing the instrumental entry points and the sixty patients were randomly allocated into one of three groups by a closed envelop data (20 patients in each group):

- Lidocaine group (L group): where 20ml of intraarticular lidocaine 1% was injected.
- Ketamine-Lidocaine group (KL group): where 1 mg/kg ketamine was injected intraarticularly in a total volume of 20ml lidocaine 1%.
- Bupivacaine group (B group): where 20ml of intraarticular bupivacaine 0.25% was injected.

Intraarticular injection of the studied drugs was done by the orthopedic surgeon using 18 G needle connected to 20ml syringe and these studied drugs were prepared and administered in a double-blind manner.

After completion of this injection, both isoflurane and N2O were discontinued and the residual neuromuscular blockade was antagonized by neostigmine and atropine.

The patients were shifted to the recovery room for close observation of hemodynamics, pain and conscious level. The postoperative observation was done by a recovery room nurse who is blind to the study design. The postoperative hemodynamics including MAP and HR was measured at 10, 20 and 30 minutes. The postoperative pain was assessed at the same time interval for hemodynamic measurements in the recovery room and at 2, 4, 6, 8, 10, 18 and 24 hours postoperatively in the ward by using VAS scores which is a 10cm scale ranging between 0=no pain and up to 10=maximum pain. If the VAS >3 iv tramadol boluses of 25mg were given until the VAS decrease to below 3 and the total tramadol consumption in 24 hours were recorded and compared. The duration of analgesia in the three groups was measured and considered to be the time elapsed between endotracheal extubation and the first postoperative analgesic request. If any disturbed conscious level, nausea or vomiting occurred, it was recorded and compared and treated accordingly.

Statistical analysis:

Data were expressed as mean ± standard deviation (SD) and median (range). The comparison between the three groups was performed by using ANOVA with post-hoc Bonferroni test. Chi square test was used for nominal data. p values <0.05 were considered statistically significant. All statistical calculations were done using computer programs Microsoft Excel version 7 (Microsoft Corporation, NY, USA).

Results

The patients in the three groups were comparable as regards age, weight and duration of surgery (Table 1).

Table (1): Demographic data in the three studied groups (mean±SD).

<table>
<thead>
<tr>
<th></th>
<th>B group (n=20)</th>
<th>L group (n=20)</th>
<th>KL group (n=20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>32.4±4.5</td>
<td>33.7±3.8</td>
<td>34.3±5</td>
</tr>
<tr>
<td>Weight (Kg)</td>
<td>74.6±6.7</td>
<td>74.1±6.5</td>
<td>72.8±4.5</td>
</tr>
<tr>
<td>Duration of surgery (min)</td>
<td>145±14.1</td>
<td>142.1±10.3</td>
<td>140±13</td>
</tr>
</tbody>
</table>

No significant difference between studied groups.

The postoperative hemodynamic parameters including MAP and HR did not show any significant changes between the studied groups at 10, 20 and 30 minutes in recovery room (Tables 2,3).
The duration of analgesia in the ketamine (KL) treated group (5.9±0.6 hr) and bupivacaine (B) group (5.6±0.8 hr) was significantly prolonged than the lidocaine (4.0±0.7 hr) only group. However, no significant changes were detected between the three studied groups as regards the total postoperative analgesic requirements in the 24 hours of study period (Table 4).

At 4 hour postoperatively, the VAS scores were lower in the ketamine-lidocaine and bupivacaine groups when compared to lidocaine group only while at 6 hour the VAS scores were higher in the TL and B groups (Table 5).

No signs of local anesthetic toxicity or changes in the level of consciousness were detected among the studied groups. Only four cases in both lidocaine and bupivacaine groups developed vomiting in-comparison to three cases in ketamine-lidocaine group (Table 4).

Table (4): Duration of analgesia, tramadol consumption and incidence of vomiting in the three studied groups [mean±SD, number (%)].

<table>
<thead>
<tr>
<th>B group (n=20)</th>
<th>L group (n=20)</th>
<th>KL group (n=20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of analgesia (hour)</td>
<td>5.6±0.8</td>
<td>4.0±0.7*</td>
</tr>
<tr>
<td>Total tramadol consumption in 24 hours (mg)</td>
<td>82.5±24</td>
<td>92.5±25</td>
</tr>
<tr>
<td>Incidence of vomiting</td>
<td>3 (15%)</td>
<td>3 (15%)</td>
</tr>
</tbody>
</table>

*p<0.05 relative to B and KL groups.

Discussion

The previous studies showed a controversial results about the beneficial effect of intraarticular local anesthetics alone in the improvement of postoperative analgesia following arthroscopic surgeries [1,12]. On the other hand, several reports suggested that the use of intraarticular adjuvants to LA reduced postoperative pain in patients undergoing these procedures. The previous studies revealed that the addition of opioids including fentanyl, sufentanil and morphine to local anesthetics extended the duration of analgesia [5,13,14] and similarly, the non opioid use in such procedures demonstrated a safe and effective pain relief [15,16].

N-methyl-D-aspartate and other glutamate receptors have been shown to present on the peripheral axons of primary afferents and peripheral injection of N-methyl-D-aspartate-receptor antagonists can suppress hyperalgesia and allodynia [17]. Ketamine is a noncompetitive antagonist of NMDA receptors that can prevent the induction of central sensitization caused by stimulation of peripheral nociception as well as blocking the wind-up phenomenon [8]. Also, it has been reported that ketamine has a local anesthetic like action through its effect on sodium channels [18]. When added to local anesthetics, ketamine through either epidural [18] or caudal [19] routes was believed to improve postoperative analgesia and decrease analgesic requirements without significant side effects. In an animal study, Zhang and his colleagues [10] recommended the use of intraarticular ketamine in humans in the management of arthritic pain after its successful application on arthritic pain behaviour in rats. While, in a recent human study, Ayoglu
and his colleagues [11] demonstrated that intrarticular ketamine together with tramadol improved postoperative analgesia without significant side effects.

This study demonstrated that the intraarticular use of ketamine 1mg/kg in a total volume of 20ml lidocaine 1% prolonged the duration of postoperative analgesia more than the use of 20ml of intraarticular lidocaine 1% alone. The duration was extended to reach a values which was insignificant to that of intraarticular bupivacaine 0.25%. The results in this study were going in hand with that of Ayoglu and his colleagues [11] in which intraarticular ketamine 0.5mg/kg when added to tramadol 50mg prolonged the duration of analgesia up to 8 hours and decreased total morphine rescue doses in 24 hours when compared to the other three groups which include the combined use of ketamine with ropivacaine or either ropivacaine or tramadol alone. Similar to that, Zhang and his colleagues [10] showed that when intraarticular ketamine 1mg and memantin 0.2mg were used in a rat model, c-Fos expression was suppressed in the laminae I-II and laminae V-VI at the L3-4 rat spinal level and subsequently reduced the associated arthritic pain-related behavior. Magnesium sulphate is a known NMDA receptor antagonist that when used in a dose of 1 gm in the study of El Sharnouby and his colleagues [20] and added to 20ml of bupivacaine 0.25% intraarticularly, it reduces postoperative pain than either drug alone.

The effective action of ketamine in this study and both ketamine and magnesium in the previous studies [11,20] suggested the occurrence of intraarticular NMDA receptors which is responsible for pain modulation inside the knee joint. In addition to that, the effect of ketamine in this study could be also explained by the sodium channel blockage action similar to that of local anesthetics [17]. Recently, NMDA receptors was believed to be another target for LA which further may explain the combined action of both lidocaine and ketamine [21].

In this study, the pain VAS scores were higher in the lidocaine 1% group at the forth hour postoperatively when compared to both ketamine-lidocaine and bupivacaine groups and this was attributed to the shorter duration of analgesia produced by intraarticular lidocaine alone. On the other hand, the pain scores at 6 hour postoperatively were higher in TL and B groups when compared to lidocaine group due to the end of analgesia duration in the latest two groups and the residual effect of tramadol which was given to the patients in lidocaine group around the 4th hour postoperatively. In accordance to that, the use of intraarticular tramadol 50mg alone resulted in an increase in the pain VAS scores earlier; at the second hour postoperatively in the study of Ayoglu et al. [11] when compared to combined tramadol and ketamine group (at 8 hour). Also, the addition of magnesium sulphate to bupivacaine in the study of El Sharnouby et al. [20] reduced VAS scores at rest and movement when compared to the treatment with bupivacaine alone.

However, the total tramadol consumption in the 24 hours postoperatively was similar between the three studied groups. Contradictory to that, the total morphine requirements in the postoperative period was reduced in the study of Ayoglu and his colleagues [11] when intraarticular ketamine was used.

After its intraarticular administration, the serum levels of bupivacaine were traced in the study of Wasudev and his colleagues [22] and revealed high levels of serum bupivacaine only when the synovial membrane was resected or divided. In their study, they recommended to decrease the dose of the injected local anesthetic if the synovium or the cartilage will be operated upon. For that reason, in this study, the total volume and concentrations of LA were revised in the previous literature and only 20ml of both lidocaine 1% and bupivacaine 0.25% were administered intraarticularly similar to that amounts given in the previous reports. In this study no signs or symptoms of LA toxicity were observed among the studied patients. Also, no significant side effects were detected between the three studied groups and that was similar to the previous studies including ketamine in intraarticular administration or regional blocks. The postoperative nausea and vomiting which occurred among the studied groups could be explained by the use of tramadol as an analgesic rescue drug.

Conclusion: When added to 20ml of lidocaine 1%, intraarticular ketamine 1mg/kg prolonged its duration more than that of lidocaine alone and it was comparable to the use of bupivacaine 0.25%. The ketamine addition was associated with better postoperative analgesia without significant side effects.

References


