Intra-articular dexmedetomidine and clonidine for postoperative analgesia in arthroscopic knee surgery

Rabinarayan Dhar¹*, Satya Prasanna Nayak²

¹Assistant Professor, Department of Orthopaedics, VIMSAR, Burla, Odisha, India
²Assistant Professor, Department of Orthopaedics, MKCG Medical College, Berhampur, Odisha, India

Received: 16 November 2016
Accepted: 02 December 2016

*Correspondence:
Dr. Rabinarayan Dhar,
E-mail: drkitusraban@gmail.com

Keywords: Dexmedetomidine, Intra-articular, Knee arthroscopy, Clonidine

ABSTRACT

Background: Many drugs have been used for postoperative pain management which is a common and distressing symptom after knee arthroscopy. But no single ideal intra-articular drug has been found. This study was done to assess the efficacy of intra-articular dexmedetomidine and clonidine for postoperative pain relief in patients undergoing arthroscopic knee surgeries.

Methods: Fifty patients of American Society of Anaesthesiologists of grade I/II, aged 20-70 years posted for arthroscopic knee surgery were randomly divided into groups I (clonidine group) and group II (dexmedetomidine group). 25 patients in group I received 1 µg/ kg of clonidine diluted to 20 ml in normal saline and group II patients received 1 µg/kg of dexmedetomidine diluted to 20 ml in normal saline via intra-articular route at the end of the surgery. Visual analogue score (VAS), time to give the first dose of analgesia and total dose of analgesic required in first 24 hours was evaluated in each group.

Results: VAS score was lower and time to first analgesic requirement was greater in Group II in comparison to Group I which was statistically significant. Total dose of analgesic used in Group II patients was significantly less compared to patients in Group I which was statistically significant.

Conclusions: Intra-articular dexmedetomidine is more effective in providing prolonged postoperative analgesia after arthroscopic knee procedures and reduces the total dose of analgesic required postoperatively compared to clonidine.

INTRODUCTION

Arthroscopic knee surgery is the commonly performed as an outpatient procedure in modern orthopaedic setup.¹ Arthroscopic knee surgery is minimally invasive and involves repair of ligaments and menisci and can evoke variable levels of pain postoperatively, which at times is very distressing for patients.² Postoperative pain can prevent early mobilization, discharge, and rehabilitation. Different intra-articular analgesic agents for day care arthroscopy have been studied but search for an ideal agent goes on. It should have rapid onset of action, have a prolonged duration of action, be easy to administer and be without serious adverse effects.³

Dexmedetomidine and clonidine are highly selective alpha2 adrenergic agonist with different sedative, anxiolytic, analgesic, and sympatholytic effects.³ They have been used intravenously and has shown to provide some analgesic effect after arthroscopic knee surgery but has produced side effects like hypotension and bradycardia.⁴ Due to paucity of studies in literature we have compared dexmedetomidine and clonidine as intra-articular analgesic in knee arthroscopic surgery.
METHODS

Approval was obtained from the ethics committee of the institution and written informed consent was obtained from the patients. Fifty patients of either sex between the age group of 20-70 years belonging to American Society of Anaesthesiologists (ASA) Class I and II undergoing elective arthroscopic knee surgery (synevection, ligament reconstruction) were included in the study. Type of anaesthetic technique was spinal anaesthesia using 2.5 ml of 0.5% hyperbaric bupivacaine. All the patients were divided into two groups I and II with 25 patients in each group. Group I was the clonidine group and Group II was the dexmedetomidine group. Group II received intra-articular dexmedetomidine 1 µg/kg diluted to 20 ml of normal saline at the end of procedure and Group I received intra-articular clonidine 1 µg/kg diluted to 20 ml of normal saline.

Patients with impaired renal and hepatic function, history of heart disease, uncontrolled hypertension, opioid or non-steroidal anti-inflammatory drug use 24 hours before surgery, cases in which drain insertion was required postoperatively were excluded from the study.

In the operating room, baseline non-invasive blood pressure, electrocardiogram, heart rate, and arterial oxygen saturation was monitored in all the patients. Visual analogue scale (VAS was explained to all patients preoperatively (0-no pain and 10-worst pain imaginable). Intravenous line was secured in all the patients. Using aseptic precautions lumber puncture was established with a midline approach at L3-4 inter space suing 25 G Quincke spinal needle and 2.5 ml of 0.5% bupivacaine (hyperbaric) was injected slowly keeping the needle orifice toward the dependent side in the lateral decubitus position which was maintained for 10 min before starting the procedure. The adequacy of spinal block was assessed and confirmed when sensory block was upto T12 level and motor block >2 score with modified Bromage scale (0-no block, 1-hip blocked, 2-hip and knee blocked, 3-hip, knee and ankle blocked) on the operative limb.

At the end of the surgery, group I patients received 20 ml clonidine solution containing clonidine as per the dose of 1 µg/kg via intra-articular route and Group II patients received 20 ml of dexmedetomidine solution containing 1 µg/kg intra-articularly minute before the release of tourniquet. Intraoperative vitals like heart rate and mean arterial pressure were noted at 5 min intervals for the first 30 min, then every 15 min till completion of surgery. Hypotension (decrease in mean arterial pressure >25% from baseline) was treated with intravenous fluids and ephedrine while bradycardia (heart rate <50 beats/min) was treated with atropine. Heart rate mean arterial pressure and pain scores (VAS) were noted at 1, 2, 4, 6, 8, 12, 18 and 24 hours postoperatively.

Intravenous paracetamol 1000 mg was administered if the VAS pain score was ≥4 and repeated at every 8 hours. Time to first analgesic dose and total dose of paracetamol was recorded during the first 24 hours in the postoperative period. Side effects such as nausea, vomiting, bradycardia, and hypotension were also noted.

Based on a pilot study with an assumption of a standard deviation of 10, a group size of 25 patients in each group was found to be sufficient to have a power of 90% for comparing VAS at 5% level of significance. Number, percentage, mean and standard deviation were used for data description. To compare the data in two groups, the t-test and Mann-Whitney test were used. SPSS version 18 was used for data analysis and p value <0.05 was considered statistically significant.

RESULTS

In this study, there was no statistically significant difference between the two groups in terms of age, sex, height, weight, ASA status and duration of surgery as shown in Table 1.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Group I</th>
<th>Group II</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>35.04±11.6</td>
<td>35±9.6</td>
<td>0.98</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>23/7</td>
<td>22/8</td>
<td>0.45</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>164.16±13.32</td>
<td>159±11.4</td>
<td>0.12</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>55.04±3.91</td>
<td>54.38±3.84</td>
<td>0.42</td>
</tr>
<tr>
<td>ASA Physical status (I/II)</td>
<td>36/14</td>
<td>35/15</td>
<td>0.57</td>
</tr>
</tbody>
</table>

Group II patients who received intra-articular dexmedetomidine showed significantly lower VAS scores at 1, 2, 4, 6, 12 and 24 hours compared to Group I patients who received intra-articular clonidine as shown in Table 2 which was statistically significant.

<table>
<thead>
<tr>
<th>VAS score-time of follow up (in hours)</th>
<th>Group I</th>
<th>Group II</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.6±1.7</td>
<td>1.26±1.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>2</td>
<td>1.7±0.5</td>
<td>1.4±1.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>4</td>
<td>2.8±0.5</td>
<td>1.3±1.76</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>6</td>
<td>3.3±0.5</td>
<td>1.2±1.38</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>12</td>
<td>4.7±0.8</td>
<td>3.9±0.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>24</td>
<td>4.9±0.6</td>
<td>4.3±0.5</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Time to first analgesic dose was also compared between the two groups and it was observed that it was significantly lesser in patients Group I (352.6±19.45 min) than Group II (380.4±24.5 min) as shown in Table 3 which was statistically significant. Duration of analgesia was prolonged in group II (360.04±11.6 min) in

Table 2: VAS score.
comparision to group I (305±19.6 min) which was statistically significant.

**Table 3: Duration and time for need of analgesia.**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Group I</th>
<th>Group II</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of analgesia (min)</td>
<td>305±19.6</td>
<td>360.04±11.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Lack of need for analgesia (no of patients)</td>
<td>18</td>
<td>23</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Need for analgesia (no of patients)</td>
<td>12</td>
<td>7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total dose of paracetamol consumption (mg)</td>
<td>1105.5±40.2</td>
<td>760.0±15.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Time to first analgesia (min)</td>
<td>352.6±19.45</td>
<td>380.4±24.5</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

The total requirement of IV paracetamol for rescue analgesia for dexmedetomidine group (760.0±15.6 mg) was significantly lower than that for the clonidine group (1105.5±40.2 mg). Overall in dexmedetomidine group only 7 patients required analgesia in the first 24 hours postoperatively in comparison to 12 in clonidine group which was statistically significant.

**DISCUSSION**

In our study, we have used intra-articular dexmedetomidine and clonidine for postoperative analgesia in patients undergoing arthroscopic knee surgeries with spinal anaesthesia as the anaesthetic technique and observed the patients for 24 hours postoperatively. The results in our study shows that intra-articular dexmedetomidine has reduced the need for postoperative pain, has reduced the total analgesic requirement, and prolonged the time to first analgesic dose requirement in comparison to intra-articular clonidine.

The mechanism of intra-articular action of dexmedetomidine is not clearly understood, but it may be similar to that suggested for clonidine. Clonidine acts on alpha 2 adrenergic presynaptic receptor and inhibits release of norepinephrine at peripheral afferent nociceptors. It has analgesic effect by inhibiting nerve impulses through C and Aδ fibers and via modulation of opioid analgesic pathway and also may stimulate the release of enkephalin-like substance at peripheral sites.

Previous studies have used in intra-articular dexmedetomidine and other drugs like morphine, fentanyl and clonidine for postop analgesia but the search for ideal drug goes on.

Al-Metwalli et al compared three groups using intra-articular dexmedetomidine, intravenous dexmedetomidine and placebo, and concluded that intra-articular dexmedetomidine in a dose of 1 µg/kg enhanced postoperative pain relief and also reduced the need for postoperative analgesia and prolonged the time to first analgesic request. These results are in agreement with our study.

El-Hamamsy et al compared intra-articular dexmedetomidine and fentanyl with bupivacaine 0.25% in a volume of 30 ml. They concluded that both dexmedetomidine and fentanyl in combination with bupivacaine resulted in increased time to first analgesic request and decreased the need for postoperative analgesia as well as increased the duration of pain relief as compared with bupivacaine alone.

Paul et al concluded that intra-articular dexmedetomidine added as an adjunct to ropivacaine in patients undergoing arthroscopic knee surgery improved the quality and duration of postoperative analgesia.

Alipour et al evaluated the efficacy of intra-articular dexmedetomidine and concluded that intra-articular dexmedetomidine in a dose of 1 µg/kg alleviates postoperative pain, reduces the need for narcotics as analgesics and increases the time to first analgesic request.

Sun et al in a meta-analysis assessed the efficacy and safety of a single dose intra-articular clonidine for postoperative pain following arthroscopic knee surgery and concluded that analgesic effect of clonidine is mild and short lasting, for just 4 h after injection suggesting that intra-articular clonidine alone could not provide sufficient postoperative analgesia which was similar to our study. Postoperative hypotension was also observed that precluded its use in ambulatory settings.

Ahmed et al concluded that intra-articular bupivacaine/dexmedetomidine provides better analgesia compared to bupivacaine/ketamine and both are superior to bupivacaine alone following knee arthroscopy.

Buerkle et al concluded in his study that most patients were very much satisfied with the postoperative analgesic regimen receiving the combination of morphine and clonidine at 24 hours postoperatively. From above studies it can be summarized that intra-articular clonidine alone cannot produce prolonged analgesia. But dexmedetomidine alone can be used as a potent intra-articular analgesic for postoperative pain management.
CONCLUSION

Intra-articular dexmedetomidine alone provides effective postoperative analgesia following arthroscopic knee surgery in comparison to intra-articular clonidine alone. Intra-articular dexmedetomidine reduced the total analgesic dose requirement and prolonged the time to need for first analgesic dose.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the institutional ethics committee

REFERENCES
