ORIGINAL ARTICLE

Is multimodal analgesia as effective as postoperative patient-controlled analgesia following upper extremity surgery?

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KEYWORDS
Postoperative pain; Multimodal perioperative analgesia; Patient-controlled analgesia

Summary
Introduction: The present prospective study compared the clinical outcomes between a multimodal analgesia group and a patient-controlled analgesia (PCA) group for postoperative pain control in upper extremities surgery.

Hypothesis: Multimodal analgesia including pre-emptive analgesic can provide similar or superior analgesic effects and a lower incidence of adverse reactions than PCA following upper extremity surgery.

Patients and methods: Sixty-one patients undergoing upper extremity surgery were randomized to 2 perioperative analgesic groups (multimodal analgesia and PCA). We compared the clinical outcomes: use of additional pain rescue, opioid-related complication rate, and patient’s satisfaction between the 2 groups.

Results: No significant differences on the resting and exercise pain scores between the two groups. Also, there were no differences regarding additional pain rescue during postoperative day (POD) 1, 2 and achievement of rehabilitation protocol in both groups. However, use of additional pain rescue in PCA group was increased significantly after PCA removal. Moreover, there was significant difference in the incidence of opioid-related complications on operation day and at POD 1. At discharge, multimodal analgesia group showed significantly greater satisfaction than PCA group.

Discussion: Perioperative pain management following upper extremity surgery through the multimodal analgesia could be an acceptable alternative method that can provide good results.

Level of evidence: Level II. Low-powered prospective randomized study.

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Introduction

Inadequate postoperative pain management has been correlated with poor functional recovery in some patients [1], and can activate a variety of biologic cascade systems, resulting in ileus, nausea, delayed mobilization and feeding, delayed hospital discharge, and unanticipated hospital readmission [2]. It is no wonder that postoperative pain remains the most common concern among patients.

The upper extremities are particularly vulnerable to injury, and thus more predisposed to surgical treatment. In addition, because the upper extremities utilize multiple joints and require fine manipulation, poor postoperative rehabilitation and a longer immobilization period can result in such complications as joint stiffness or complex regional pain syndrome, which negatively impact patients’ functional outcomes.

A range of techniques have been used to provide postoperative analgesia, including non-steroidal anti-inflammatory drugs (NSAIDs) and patient-controlled analgesia (PCA), epidural or intrathecal opioids, and local anesthetic agents. Opioids are considered the cornerstone for treatment of moderate-to-severe acute postoperative pain [3], and PCA is the mode most frequent of postoperative opioid administration [4]. Although highly efficacious, unwanted adverse effects, such as ventilatory depression, drowsiness, sedation, nausea, vomiting, pruritus, urinary retention, ileus, and constipation are frequently observed during opioid PCA [5]. Because of these unwanted adverse effects, PCA is often discontinued despite insufficient pain management [6]. Patients consider nausea and vomiting to be the most undesirable postoperative complications [7], and are willing to pay more than $50 to avoid them [8]. Moreover, nausea and vomiting delay patients’ return to oral feeding, recovery, and hospital discharge. Other adverse effects of opioids similarly impair active mobilization and rehabilitation [9].

Multimodal analgesia, using a combination of analgesics throughout the perioperative period, to control postoperative pain has become increasingly popular and well accepted [10,11]. The rationale for this strategy is the achievement of sufficient analgesia caused by the additive or synergistic effects of different classes of analgesics [12]. Multimodal analgesia has been proposed to decrease opioid consumption and to improve postoperative analgesia after severely painful surgery. A lower incidence of adverse effects and improved analgesia have been demonstrated with multimodal analgesic techniques, which may lead to shorter hospitalization times, improved recovery and function, and possibly decreased healthcare costs [13]. However, studies on postoperative pain management via multimodal analgesia have been limited to hip and knee arthroplasty, spine surgery, or major operations such as cardiac, abdominal, or cancer surgery. Few studies have been conducted on postoperative pain management of the upper extremities.

The present working hypothesis was that multimodal analgesia including pre-emptive analgesic can provide similar analgesic effects and a lower incidence of adverse effects than PCA, and this method has similar clinical outcomes as PCA following upper extremity surgery, focusing on:

- clinical outcomes;
- complication rate;
- administration of additional pain rescue;
- patient satisfaction.

Patients and methods

We prospectively compared the intensity of pain (independent evaluator) for principal evaluation criteria, and functional outcome (Mayo Elbow Performance Score [MEPS]), complication of opioids and multimodal analgesics and patient satisfaction for secondary evaluation criteria between a group of patients who received multimodal analgesia including pre-emptive analgesics and a group of patients who used PCA for postoperative pain control from February 2009 to October 2011.

Patients and evaluations

Among upper extremity surgeries, those around the elbow, which are associated with relatively more severe perioperative pain and require early rehabilitation, were selected for the comparison of patients with the same conditions in this study. The inclusion criteria were as follows:

- fracture around the elbow and dislocation, multiple elbow ligament injuries, or severe osteoarthritis (OA) of the elbow, which was treated with ulno-humeral arthroplasty or total elbow arthroplasty;
- ability to undergo axillary brachial plexus block (BPB);
- no neurologic symptoms involving the upper extremities;
- normal upper extremity function before injury.

The exclusion criteria included the following: renal insufficiency; severe systemic arthritis; rheumatoid arthritis; diabetes with significant peripheral neuropathy; contraindications (e.g., localized infection, sepsis, or pre-existing neurologic abnormality involving the upper extremities); patient refusal of either BPB or IV-PCA; allergy to local anesthetics, morphine, or oxycodone; chronic opioid use; multiple traumas; pathologic fracture; history of PCA discontinuation due to adverse effects; and difficulty comprehending the VAS or how to use the IV-PCA device.

A total of 63 patients were selected initially, but 2 were excluded because of inadequate BPB anesthesia, with a conversion to general anesthesia intraoperatively (1 each in groups, A and B). Therefore, 61 patients comprising of 37 women and 24 men, with a mean age of 53 years (range, 21–78 years) were enrolled in this study. Their demographics and general medical information were obtained (Table 1). The clinical pathway and randomization process were explained. The patients were randomized into 2 groups using a computer-generated random number and a sealed envelope design: group A (n = 30) received multimodal analgesia including pre-emptive analgesics (cyclooxygenase-2 (COX-2) inhibitor, pregabalin, and NSAIDs orally), whereas group B (n = 31) received IV-PCA postoperatively, without pre-emptive analgesics.
Multimodal analgesia for upper extremity surgery

Table 1  Demographics and general medical information.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Group A</th>
<th>Group B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients (n)</td>
<td>30</td>
<td>31</td>
</tr>
<tr>
<td>Injury type (n)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Distal humerus fracture</td>
<td>19</td>
<td>21</td>
</tr>
<tr>
<td>Elbow fracture and dislocation</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Multiple elbow ligament injuries</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Osteoarthritis</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>Gender (M/F)</td>
<td>13/17</td>
<td>11/20</td>
</tr>
<tr>
<td>Age (years)</td>
<td>52.3 (10)</td>
<td>54.1 (11)</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>169.3 (11)</td>
<td>168.7 (9)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>63 (13)</td>
<td>64 (11)</td>
</tr>
<tr>
<td>Body Mass Index (kg/m²)</td>
<td>24 (3)</td>
<td>25 (3)</td>
</tr>
</tbody>
</table>

Values are mean (±SD).

Analgesic management

Various regimens of multimodal analgesia including pre-emptive analgesics have been introduced [14, 15]. Common medications include NSAIDs, COX-2 inhibitor, ketamine, local anesthetics, α2-agonist, and α2δ-ligands [16]. The current pain management regimen at our hospital utilizes some of these available agents [17]. One hour before surgery, when patient was called into the operating room, the patients in group A received pre-emptive treatment with NSAIDs (ibuprofen 800 mg), COX-2 inhibitor (celecoxib 400 mg), pregabalin 75 mg with a little water.

All patients were operated under BPB anesthesia administered by a senior anesthetist. Before incision and after skin closure, the skin, subcutaneous tissues, and periosteum of incision site in all patients were injected with a 40 mL mixture of normal saline 450 mL, 0.75% ropivacaine 40 mL, ketorolac 30 mg, and epinephrine 0.5 mg.

The patients in group A received ibuprofen 800 mg, celecoxib 400 mg, and pregabalin 75 mg 2 hours after the surgery. From postoperative day (POD) 1, the patient in group A received this same regimen twice daily for 2 weeks. Whereas the patients in group B received IV-PCA postoperatively, this was initiated in the recovery room. IV-PCA (butorphanol 4 mg, ketorolac 150 mg, and normal saline 50 mL), which was programmed to deliver a 1 mg bolus (lock-out of 10 min) with a maximum dose of 6 mg/h, was available to all the patients in group B, who were instructed to titrate their VAS pain scores to ≤3 out of 10 until the morning of POD 3. On POD 3, IVPCA was discontinued. All the patients in groups A and B received oxycodone hydrochloride (HCl) 10 mg every 12 hours and acetaminophen 650 mg 3 times daily postoperatively (oxycodone HCl for 1 week, acetaminophen for 2 weeks). Any breakthrough pain (defined as ≥4/10 on the VAS) after surgery was controlled on demand with IV paracetamol 2 g administered 4 times daily and additional oxycodone HCL 10 mg administered every 12 hours in both the groups (Table 2).

Rehabilitation

A scheduled range of motion (ROM) exercise rehabilitation protocol was set for elbow ROM after surgery in both the groups. Rehabilitation following elbow surgery follows a sequential and progressive multiphased approach consisting of an immediate motion phase (week 1), intermediate phase (weeks 2—4), advanced strengthening phase (weeks 4—8), and return-to-activity phase (weeks 8—12) (Table 3) [18—20]. Elbow ROM exercises are initiated as tolerated the day after surgery under the supervision of a physiotherapist. The patients were discharged after a 2-week hospitalization, and then followed-up at 4, 8, and 12 weeks to examine their achievement. Subsequently, patients were trained on the subsequent protocol and preceded to the next phase. After 6 months, the physiotherapist evaluated the functional outcomes of the elbow of all the patients.

Assessments

The intensity of postoperative pain was assessed using the 100-mm VAS pain scale ruler, which ranged from 0 (no pain) to 100 (worst pain imaginable). A single evaluator, who was not involved in and unaware of the concepts and

Table 2  Protocols for postoperative pain management in group A and B.

<table>
<thead>
<tr>
<th>Period</th>
<th>Group A</th>
<th>Group B</th>
<th>Common</th>
<th>As required</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-emptive</td>
<td>Ibuprofen 800 mg</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td>Celecoxib 400 mg</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td>Pregabalin 75 mg</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Operation day</td>
<td>Ibuprofen 800 mg</td>
<td>—</td>
<td>Oxycodone HCl 10 mg</td>
<td>IV paracetamol 2 g</td>
</tr>
<tr>
<td></td>
<td>Celecoxib 400 mg</td>
<td>—</td>
<td>every 12 hours</td>
<td>Oxycodone HCL 10 mg</td>
</tr>
<tr>
<td></td>
<td>Pregabalin 75 mg</td>
<td>—</td>
<td>Acetaminophen 650 mg</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2 hours after surgery</td>
<td>IV-PCA in recovery</td>
<td>3 times daily</td>
<td></td>
</tr>
<tr>
<td>POD 1—3</td>
<td>Ibuprofen 800 mg</td>
<td>—</td>
<td>Same as above</td>
<td>Same as above</td>
</tr>
<tr>
<td></td>
<td>Celecoxib 200 mg</td>
<td>—</td>
<td>Acetaminophen 650 mg</td>
<td>Same as above</td>
</tr>
<tr>
<td></td>
<td>Pregabalin 75 mg</td>
<td>—</td>
<td>3 times daily</td>
<td>Same as above</td>
</tr>
<tr>
<td></td>
<td>twice daily</td>
<td>—</td>
<td></td>
<td></td>
</tr>
<tr>
<td>POD 3—7</td>
<td>Same as above</td>
<td>—</td>
<td>Same as above</td>
<td></td>
</tr>
<tr>
<td>POD 7—14</td>
<td>Same as above</td>
<td>—</td>
<td>Acetaminophen 650 mg</td>
<td>Same as above</td>
</tr>
</tbody>
</table>

POD: postoperative day; IV: intravenous; PCA: patient controlled analgesia; HCl: hydrochloride.
Table 3 Scheduled ROM exercise rehabilitation protocol.

<table>
<thead>
<tr>
<th>Phase</th>
<th>Goals: full wrist and elbow ROM, decrease swelling</th>
</tr>
</thead>
</table>
| POD 2 | Remove bulky dressing and replace with elastic bandages  
         Immediate hand, wrist, and elbow exercises  
         Grip strengthening  
         Wrist flexor and extensor stretching  
         Pronation/supination |
| POD 3 to 7 | Passive ROM elbow extension/flexion (motion to tolerance)  
            Begin progressive resisted exercises (PRE) |

Intermediate phase (weeks 2–4)

<table>
<thead>
<tr>
<th>Goals: improve muscular strength and endurance, normalize joint arthrokinematics</th>
</tr>
</thead>
</table>
| Week 2 | ROM exercises (overpressure into extension)  
         Continue to progress PRE weight and repetitions as tolerable |
| Week 3 | Initiate biceps and biceps eccentric exercise program  
         Initiate rotator cuff exercises program |

Advanced strengthening phase (weeks 4–8)

<table>
<thead>
<tr>
<th>Goals: gradually increase strength, power, endurance, and neuromuscular control in order to prepare for a gradual return to sport</th>
</tr>
</thead>
</table>
| Weeks 4–6 | Aggressive strengthening exercises, emphasizing high speed and eccentric contraction  
            Resistance applied for concentric and eccentric contractions of the elbow flexors  
            Aggressive strengthening exercises with weight machines |
| Weeks 7–8 | Neuromuscular control exercises progress  
            Initiate plyometric exercises program |

Return-to-activity phase (weeks 8–12)

<table>
<thead>
<tr>
<th>Goal: progressively return to full competition sport activities</th>
</tr>
</thead>
</table>
| Exhibit full ROM with no pain or tenderness  
| Ensures maintenance of necessary ROM and flexibility of the shoulder joint |

ROM range of motion, POD postoperative day.

method of this study, determined the VAS score for each patient. On operation day, the VAS score was recorded at 6 and 12 hours after surgery. From POD 1, the resting pain score was measured at 9:00 and 18:00 for resting, and from POD 2, when ROM exercise was initiated, the exercise pain score was measured at 11:00 and 20:00. We used the average of the VAS measurements each for resting and exercise. Achievement of ROM exercise was measured by a blinded, independent physiotherapist. Once the patient initiated ROM exercise according to the scheduled ROM exercise rehabilitation protocol on POD 2, the physiotherapist assessed when the scheduled ROM exercise could be conducted by the patient, and whether additional pain rescue was required to conduct the scheduled ROM exercise. In addition, after the 6-month follow-up, the physiotherapist evaluated the functional outcomes of the elbow. The functional outcomes were assessed using the MEPS [21]. In the MEPS system, pain (45 points), motion (20 points), stability (10 points) and function (25 points) were evaluated. The ROM of the elbow was evaluated using a goniometer. The functional arc of flexion–extension, as determined based on a flexion–extension arc of 30° to 130°, and 100° of forearm rotation [22], and the range of pronation and supination were evaluated with the elbow flexed 90°, and compared with the range of motion of the contralateral side (as a percentage).

The complications of opioids and multimodal analgesic drugs were noted as present or absent, according to the use of medication. The following were recorded: postoperative nausea or vomiting requiring antiemetic drugs, constipation requiring laxatives, urinary retention requiring the placement of a catheter, and drowsiness when normal activities or physiotherapy could not occur because the patient was too sleepy.

Patient satisfaction with the analgesia was assessed on the day of discharge using a 4-point scale: insufficient, 4
points; satisfactory, 3 points; good, 2 points; or very good, 1 point.

Statistics

The differences between the two groups were assessed using the Wilcoxon signed-rank test for pain score, functional outcomes of the elbow, and patient satisfaction, and Fisher's exact test for complications, achievement of scheduled ROM exercise, and administration of additional pain rescue. Statistical analysis was performed using SPSS version 20.0 software (IBM Corporation, Armonk, NY). A P-value of < 0.05 was considered statistically significant.

Results

The resting pain scores of group A were lower than those of group B, there was no significant difference between the 2 groups (P = 0.655, 0.089, 0.597, 0.783, 0.988, 0.692, 0.785, 0.942, 0.992 at 6 and 12 hours after surgery, and on PODs 1 to 14, respectively) (Fig. 1). In group A, the exercise pain scores gradually decreased as time passed. Meanwhile, in group B, they smoothly decreased upon PCA removal on POD 3, and gradually decreased thereafter. Although the exercise pain scores of group B were higher than those of group A, the difference was not statistically significant (P = 0.068, 0.623, 0.598 at PODs 3 to 14, respectively) (Fig. 2).

No significant difference in additional pain rescue was found between the two groups on operation day, POD 1 and 2 (P = 0.73, > 0.99, > 0.99, respectively). However, the additional pain rescue increased significantly in group B after PCA removal (P = 0.014 and 0.012 on PODs 3 and 4, respectively). No difference in the achievement of rehabilitation protocol was observed between the 2 groups (P > 0.99) (Fig. 3). There was a significant difference in the incidence of opioid-related complications on operation day and POD 1 (P = 0.018 and 0.037, respectively) (Fig. 4).

Complications of multimodal analgesic drugs (pregabalin, NSAIDs), such as headache, dizziness, and somnolence were not reported by any patients in group A. At discharge, the patients in group A showed a significantly greater satisfaction with their method of analgesia than the patients in group B (P = 0.001): group B scored 2.0 (range, 2.0–3.0), whereas group A scored 1.0 (range, 1.0–2.0).

The functional outcomes were measured at 6-month follow-up. The functional outcomes were similar in the two groups (P > 0.99) (Table 4).

Discussion

The results of this study showed that the opioid-related complication rate was significantly lower in group A than in group B on operation day and POD 1. In particular, the treatment was effective in reducing postoperative nausea and vomiting, which tend to be severest on operation day and POD 1 [9], and most significantly affect patient satisfaction [7]. In most previous studies, no limit was set to the
Table 4 Functional outcomes at 6 months follow-up.

<table>
<thead>
<tr>
<th>Injury type</th>
<th>Group A</th>
<th>Group B</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Distal humerus fracture</td>
<td>flex-ext: 122 ± 7°</td>
<td>flex-ext: 125 ± 11°</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td></td>
<td>pro/sup: 158 ± 10°</td>
<td>pro/sup: 154 ± 7°</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td></td>
<td>MEPS: 88 ± 8.4</td>
<td>MEPS: 85 ± 5.4</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td>Elbow fracture and dislocation</td>
<td>flex-ext: 121 ± 11°</td>
<td>flex-ext: 122 ± 9°</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td></td>
<td>pro/sup: 153 ± 7°</td>
<td>pro/sup: 155 ± 6°</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td></td>
<td>MEPS: 90 ± 7.4</td>
<td>MEPS: 88 ± 8.4</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td>Multiple elbow ligament injury</td>
<td>flex-ext: 127 ± 6°</td>
<td>flex-ext: 124 ± 9°</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td></td>
<td>pro/sup: 159 ± 5°</td>
<td>pro/sup: 158 ± 9°</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td></td>
<td>MEPS: 90 ± 5.2</td>
<td>MEPS: 89 ± 7.9</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td>Osteoarthritis</td>
<td>flex-ext: 135 ± 14°</td>
<td>flex-ext: 133 ± 12°</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td></td>
<td>pro/sup: 146 ± 11°</td>
<td>pro/sup: 148 ± 8°</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td></td>
<td>MEPS: 85 ± 8.8</td>
<td>MEPS: 87 ± 8.6</td>
<td>&gt;0.99</td>
</tr>
</tbody>
</table>

Values are mean (±SD); flex: flexion; ext: extension; pro: pronation; sup: supination; MEPS: Mayo Elbow Performance Score.

Figure 4 Graph display the opioid-related complication rate from operation day to postoperative (POD) 4. The values are expressed as the percentage of patients and the number of patients in detail. Patients in group B reported significantly more opioid-related complications on operation day and POD 1 (P = 0.018 and 0.037, respectively). N/V: nausea and vomiting; cons: constipation; UR: urinary retention; drow: drowsiness; *: statistically significant.

The use of opioids administered of PCA system [9]. Although the IV-PCA system used in this study had a bolus dose of 1 mg, a lock-out interval of 10 min, and a maximum dose of 6 mg/h, 44% of the patients reported adverse effects. The multimodal analgesia used in this study significantly decreased opioid-related complications. Furthermore, we observed no significant difference in the postoperative analgesic effect in both groups. IV-PCA can be used in the recovery room immediately following surgery. In addition, medication can be continued during the use of IV-PCA, and if desired by a patient, immediate pain management can be achieved via bolus dose. However, unlike multimodal analgesia, which enables constant pain control for 2 weeks, IV-PCA is removed on POD 2 or 3, if postoperative pain decreases.

Pain evaluation generally is performed in a resting state with the use of the VAS. However, this evaluation does not consider unexpected peaks in pain that occur after ROM exercise. Patients feel more pain when they conduct ROM exercise, and this pain can increase their fear and decrease their motivation for ROM exercise, leading to poor postoperative clinical outcome caused by improper ROM exercise. As shown in this study, the removal of IV-PCA on POD 3 did not affect the resting pain scores, but did affect the exercise pain scores. After the removal of IV-PCA, the administration of additional pain rescues increased significantly required in group B. Furthermore, the achievement of scheduled ROM exercise was similar between the 2 groups during their 2-week hospitalization. This means that more additional pain rescue was required in group B to obtain the similar clinical outcomes of group A.

There were as few limitations of this study. First, the pharmacokinetics and effective dose of multimodal analgesia were not determined. Therefore, outcomes may vary depending on the regimen utilized. Second, unlike IV-PCA, multimodal analgesia including pre-emptive analgesics has the disadvantage of having to administer medication at a fixed time. If patient compliance is low, it can cause poor pain management due to a difference in medication time and dose. Third, the subjects of this study were restricted to patients who could undergo axillary BPB. The residual effect of BPB could affect acute postoperative pain. Besides, in the case of general anesthesia, perioperative pain management could be difficult as medication is unavailable for fasting period.

Conclusion

In surgery associated with intense postoperative pain, successful postoperative pain management is difficult to achieve without the PCA, despite its complications. However, we found that multimodal analgesia including pre-emptive analgesics for perioperative pain management in upper extremity surgery had a lower complication rate and additional pain rescue, and had similar analgesic effects and functional outcomes, compared with IV-PCA. As shown in this study, multimodal analgesia including pre-emptive analgesics can be useful and an acceptable alternative in upper extremity surgery, which is associated with relatively lower postoperative pain.
Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

References