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JA SYMPOSIUM

Postoperative analgesia

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Achieving analgesia not only at rest but also during movement, with the minimization of unpleasant symptoms related to analgesics, is one of the goals of postoperative analgesia (POA). "Multimodal analgesia" or "balanced analgesia", advocated by Kehlet and Dahl from the 1990s [1], is thought to be the most important concept for achieving this goal. The rationale for this concept is the achievement of sufficient analgesia brought about by additive or synergistic effects between different analgesics, with the concomitant reduction of side effects, due to the resulting lower doses of analgesics and differences in side-effect profiles. The paper will briefly review the utility of the multimodal technique in epidural analgesia (EA), mainly demonstrating the results of our clinical investigations, and will discuss the benefits and risks of EA and intravenous patient-controlled analgesia (IV-PCA), the clinical implications of EA, and future directions of multimodal POA.

In Japan, EA has played a central role in POA for more than a quarter of a century. Some anesthesiologists had extended its indications to the breast and upper extremities surgery, as well as thoracic, abdominal, hip, and knee surgery. Because the subjective perception of postoperative pain is different for each individual, PCA is a rational and effective method for POA for achieving the patient's desired level of analgesia by their operating a programmed pump. Although EA has been widely used in Japan and the theoretical utility of IV-PCA has been noted, IV-PCA had not become common in Japan until a few years ago. A PCA system was introduced into epidural POA in the 1990s, and we started patient-controlled epidural analgesia (PCEA) after gynecological surgery in 1997. In our earlier regimen, PCEA was started after the epidural injection of 0.25% bupivacaine 8 mL, and consisted of a solution containing buprenorphine 10 μg/ml and droperidol 0.1 mg/ml. The PCEA device was programmed to deliver a 2 ml bolus with a 15 min lockout interval without background infusion. While this regimen provided preferable analgesia at rest, we found several problems; some patients complained of pain immediately after surgery and they frequently used PCEA boluses, and some patients complained of severe dynamic pain. Therefore, we performed a series of clinical investigations to solve these problems.

At first, we confirmed that the addition of buprenorphine 0.1 mg to an epidural bolus injection of 0.25% bupivacaine 8 ml prior to the start of PCEA significantly decreased PCEA boluses immediately after surgery [2]. Next, to

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investigate the role of additional local anesthetic in the PCEA solution, we assessed the efficacy and side effects of adding 0.1% bupivacaine to our PCEA solution. The result of this study was that median visual analogue pain scores (VAPS) on coughing in patients who received the additional 0.1% bupivacaine were significantly lower, although VAPS at rest and the cumulative consumption of the PCEA solution were similar [3]. Furthermore, as a part of multimodal analgesia, we evaluated the effect of a parenteral nonsteroidal anti-inflammatory drug (NSAID) given before the start of PCEA. Rectal diclofenac 50 mg administered immediately after gynecological surgery significantly decreased the number of PCEA boluses during the first postoperative 16 h (Fig. 1) [4]. The results of these studies demonstrated that multimodal transitional analgesia using a parenteral NSAID plus the combination of epidural local anesthetic and opioid, followed by PCEA using a mixture of local anesthetic and opioid was a better choice for epidural POA.

Postoperative nausea and vomiting (PONV) is an as yet unsolved problem, and some patients who have experienced such unpleasant symptoms underestimate the value of the modality of POA. Epidural droperidol mixed with local anesthetic and opioid has been widely used in Japan for preventing PONV. However, its anti-emetic effect has not been fully evaluated. Thus, we compared the effect of adding droperidol 0.1 mg/ml to PCEA solution with 0.1% bupivacaine and buprenorphine 10 μg/ml after gynecological surgery. The PCEA device was programmed to deliver a 2 ml bolus with a 15 min lockout interval without background infusion. The result showed that the additional droperidol significantly reduced the intensity of nausea at 6

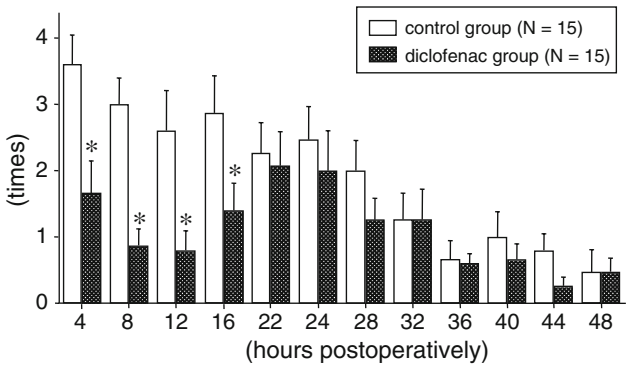

Fig. 1 Mean numbers of bolus injections of postoperative patient-controlled epidural analgesia (PCEA) during first 48 postoperative hours. The PCEA device was programmed to deliver a 2 ml bolus with a 15 min lockout interval without background infusion with solution containing 0.1% bupivacaine, buprenorphine 10 μg/ml, and droperidol 0.1 mg/ml. The diclofenac group received rectal diclofenac 50 mg and the control group received no medication at the end of surgery. $*P < 0.05$ compared with the control group with t test. This result was presented at the Annual Meeting of the American Society of Anesthesiologists in 1999

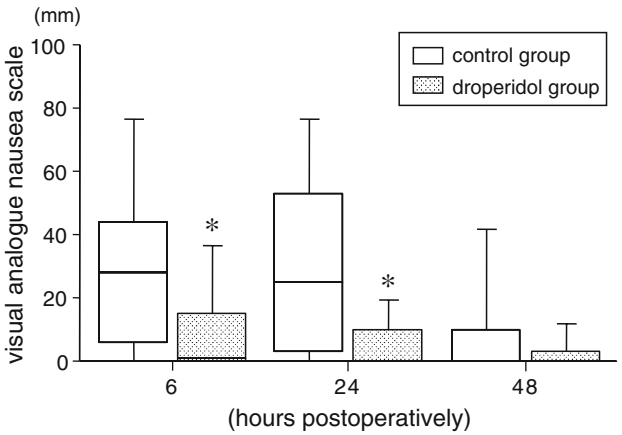

Fig. 2 Median visual analogue scale for nausea (0 = no nausea, 100 = worst nausea) at 6, 24, and 48 h after surgery. $*P < 0.05$ compared with the control group with the Mann–Whitney test. The control group received postoperative patient-controlled epidural analgesia using 0.1% bupivacaine and buprenorphine 10 μg/ml, and the droperidol group received postoperative PCEA using 0.1% bupivacaine, buprenorphine 10 μg/ml, and droperidol 0.1 mg/ml. The PCEA device for both groups was programmed to deliver a 2 ml bolus with a 15 min lockout interval without background infusion. This result was presented in Annual Meeting of American Society of Anesthesiologists in 2000

and 24 h postoperatively (Fig. 2) [5]. However, although droperidol has an anti-emetic effect, it can cause extrapyramidal symptoms and QT prolongation. Therefore, its benefits and risks must be carefully considered, and we have not added droperidol to epidural solution in our recent clinical practice.

In 2001, ropivacaine became commercially available in Japan, and a series of multicenter clinical studies were performed. In patients who received continuous epidural infusion (CEI) combined with epidural morphine 3 mg/day after upper abdominal surgery, three different concentrations and speeds of epidural ropivacaine, 0.2% at 4 ml/h, 0.1% at 8 ml/h, and 0.133% 8 ml/h, were examined. The results showed that all the solutions provided preferable analgesia both at rest and movement and the incidences of hypotension and PONV were higher in patients who received 0.133% at 8 ml/h. The extension of analgesic segments narrowed as time passed and approximately half of the patients required supplemental analgesic during the early postoperative period. These results support the utility of a combination of a local anesthetic and an opioid in epidural bolus prior to CEI and the addition of PCA to CEI.

The choice and optimal dose of opioid in PCEA is still open to discussion. Lipophilicity is an important factor for the choice. Less lipophilic opioids such as morphine are advantageous in providing longer duration and a wider area of analgesia. However, there are several disadvantages of their use in PCEA; the onset of analgesia is

slower and the incidences of nausea and pruritus are higher than with lipophilic opioids, and delayed wider intrathecal rostal spread could potentially cause delayed respiratory depression. On the other hand, lipophilic opioids such as fentanyl tend to be preferred because of their rapid onset and less frequent unwanted symptoms. A textbook states that the epidural bolus dose and daily dose of morphine for CEI range from 1 to 5 mg and 2.4 to 24 mg/day, respectively [6]. However, we have noticed that these doses were overdosages for some patients. In addition, PCEA provides similar analgesia with lower drug consumption than CEI [7, 8]. Therefore, we evaluated the analgesic efficacy and side effects of two different concentrations of morphine (12.5 or 25 μg/ml) with a mixture of 0.2% ropivacaine in PCEA (continuous infusion 4 ml/h, bolus injection 2 ml, lockout interval 15 min) following the epidural injection of 0.375% ropivacaine 8 mL plus morphine 1 mg, in gynecological patients [9]. There were no significant differences in analgesia either at rest or during movement, and there were no differences in the cumulative boluses of PCEA (3.4 vs. 4.3 times per 48 h). The incidences of PONV, pruritus, and leg numbness were greater in the morphine 25 μg/ml group, though statistically insignificant. Accordingly, we concluded that a lower morphine concentration is a better choice in PCEA with respect to analgesic efficacy and the potential risk of side effects [9]. The concentration of fentanyl used in PCEA varies among institutions in Japan, and finding the optimal concentration is thought to be a further subject to be addressed in POA.

Postoperative EA has been thought to be beneficial for patients, and has been a very common modality for POA in Japan. Metaanalyses confirm the advantages of postoperative EA; it provides statistically superior analgesia to both mixed systemic and IV-PCA delivery of opioid for at least the first three postoperative days for a variety of surgical procedures [10], it could reduce postoperative cardiovascular and pulmonary complications after major vascular surgery and in high-risk patients [11], and EA with local anesthetics hastened the return of postoperative gastrointestinal function after abdominal surgery by 24–37 h [11]. However, there is a lack of high-quality data on the effects of different analgesic techniques and regimens on health-related quality of life, quality of recovery, and patient satisfaction [10]. In addition, we can never ignore the extremely rare but catastrophic irreversible central nerve damage caused by EA. The recent increase in the number of patients who require continuous anti-coagulation therapy for ischemic diseases and aggressive pharmacological prevention of perioperative thromboembolic events restricts the application of EA. Moreover, the number of minimum invasive surgeries has been increasing in the past decade. In this circumstance, where should our POA go? Should we persist in EA or enlarge the indications for IV-PCA to major surgery? I believe that the answers to both questions are "No".

During the last few years, locoregional analgesia techniques have been widely applied to POA. A metaanalysis by Joshi et al. [12] demonstrated that continuous paravertebral block was as effective as thoracic EA but was associated with a reduced incidence of hypotension after thoracotomy. McDonnell et al. [13–15] demonstrated that the transversus abdominis plane block, as a component of multimodal analgesia, provided superior analgesia with less intravenous morphine consumption compared to placebo block after various elective abdominal surgeries. In a recent few years, although it is unpublished, we observed that multimodal postoperative analgesia using peripheral nerve block, IV-PCA with morphine, and intravenous NSAID provided preferable analgesia at rest and could allow more than half of patients who received thoracic or abdominal surgery ambulated on postoperative day 1. These findings encourage us and warrant further clinical evaluation for comparing multimodal analgesia using locoregional analgesia and conventional EA.

The concept of "context-sensitive analgesia" advocated by Fanelli et al. [16] is agreeable. It includes the concept of multimodal analgesia and means that analgesia should be instituted as early as deemed necessary to avoid persistent pain, and it should be continued, with different modalities, until full recovery from surgery [16]. In this type of analgesia, pathophysiological and biochemical comprehensions regarding the type of surgery and its associated pain have to be considered. Anti-inflammatory agents and anti-neuropathic agents must play important roles in this concept, in addition to local anesthetics and opioids. Moreover, we have to recognize that not only analgesia but also outcome improvement, such as an expedited return to social life and daily activities, is also an important goal of POA.

Conclusions and future perspectives

1. Pharmacological multimodal analgesia with epidural local anesthetic and opioid, plus an NSAID, play a central role in POA for patients who have received EA. Although EA has several advantages over IV-PCA, its indications have to be reconsidered.
2. Multimodal analgesia combined with regional analgesia, IV-PCA, and an NSAID could be an alternative to EA in certain circumstances.
3. We have to focus not only on pain scores but also on postoperative outcome as the goal of POA. To achieve this purpose, the concept of context-sensitive analgesia should be borne in mind.

References

1. Kehlet H, Dahl JB. The value of "multimodal" or "balanced analgesia" in postoperative pain treatment. Anesth Analg. 1993;77:1048–56.
2. Inoue S, Hiruta M, Kawakami T, Hiruta A, Hirabayashi Y, Seo N. Epidural single injection of the combination of 0.25% bupivacaine and buprenorphine reduced the request of patient-controlled epidural analgesia during early postoperative period (in Japanese). Pein Kurinikku Pain Clinic. 2004;25:339–43.
3. Inoue S, Mitsuhata H, Kawakami T, Shimohata K, Hirabayashi Y, Seo N. Addition of 0.1% bupivacaine to buprenorphine and droperidol in patient-controlled epidural analgesia improved postoperative pain scores on coughing after gynecological surgery. J Clin Anesth. 2005;17:167–71.
4. Inoue S, Hirabayashi Y, Shimohata K, Akazawa S, Shimizu R. Rectal diclofenac reduced the drug consumption in the patient-controlled epidural analgesia after gynecological surgery. Anesthesiology. 1999;91:A936.
5. Inoue S, Hiruta M, Suzuki H, Seo N. Antiemetic effect of simultaneous epidural administration of droperidol during patient-controlled analgesia. Anesthesiology. 2000;93:A942.
6. Wu CL. Acute postoperative pain. In: Miller RD, editor. Miller's Anesthesia. Sixth edition ed. Philadelphia: Elsevier Churchill Livingstone; 2005. p. 2729–62.
7. Boudreault D, Brasseur L, Samii K, Lemoing JP. Comparison of continuous epidural bupivacaine infusion plus either continuous epidural infusion or patient-controlled epidural injection of fentanyl for postoperative analgesia. Anesth Analg. 1991;73:132–7.
8. Marlowe S, Engstrom R, White PF. Epidural patient-controlled analgesia (PCA): an alternative to continuous epidural infusions. Pain. 1989;37:97–101.
9. Inoue S, Kawakami T, Seo N. Comparison of the concentration of morphine for patient-controlled epidural analgesia following gynecological surgery. Minerva Anestesiol. 2009;75:498–503.
10. Liu SS, Wu CL. The effect of analgesic technique on postoperative patient-reported outcomes including analgesia: a systematic review. Anesth Analg. 2007;105:789–808.
11. Liu SS, Wu CL. Effect of postoperative analgesia on major postoperative complications: a systematic update of the evidence. Anesth Analg. 2007;104:689–702.
12. Joshi GP, Bonnet F, Shah R, Wilkinson RC, Camu F, Fischer B, Neugebauer EAM, Rawal N, Schug SA, Simanski C, Kehlet H. A systemic review of randomized trials evaluating regional techniques for postthoracotomy analgesia. Anesth Analg. 2008;107:1026–40.
13. McDonnell JG, Curley G, Carney J, Benton A, Costello J, Maharaj CH, Laffey JG. The analgesic efficacy of transversus abdominis plane block after cesarean delivery: a randomized controlled trial. Anesth Analg. 2008;106:186–91.
14. Carney J, McDonnell JG, Ochana A, Bhinder R, Laffey JG. The transversus abdominis plane block provides effective postoperative analgesia in patients undergoing total abdominal hysterectomy. Anesth Analg. 2008;107:2056–60.
15. McDonnell JG, O'Donnell B, Curley G, Heffernan A, Power C, Laffey JG. The analgesic efficacy of transversus abdominis plane block after abdominal surgery: a prospective randomized controlled trial. Anesth Analg. 2007;104:193–7.
16. Fanelli G, Berti M, Baciarello M. Updating postoperative pain management: from multimodal to context-sensitive treatment. Minerva Anestesiol. 2008;74:489–500.