Editorial Commentary

Long acting local anesthesia and preventive analgesia—difficulty of prove on clinical trial

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Owing to effective anesthetic agents and improved methods of anesthesia, nowadays, patients feel almost no pain during extractions. However, postoperative pain continues to cause discomfort and distress to many patients. Nonsteroidal anti-inflammatory drugs (NSAIDs) and opioids are often prescribed post-extraction. However, because NSAIDs may cause ulcers, they must be used with caution in patients with gastrointestinal disease. Furthermore, they cannot be administered to patients who have aspirin intolerance, which has become an issue in the recent years. The addictive nature of opioids also makes it difficult to prescribe them in sufficient doses. Therefore, alternative methods for alleviation of postoperative pain are being investigated. Animal studies have explored the use of preventive (also called pre-emptive) analgesia and have reported that adequate pre-operative analgesia can confer effective post-operative pain relief (1-4). However, results of clinical studies have been inconsistent, with some reporting that preventive analgesia was effective (5,6) but others showing negative results (7-9). The reasons for these conflicting observations may be individual differences in pain thresholds and psychological factors.

The study of Amorim *et al.* titled "Postoperative analgesia in extraction of impacted mandibular third molars? A randomized clinical trial" was well-designed and showed that the long-acting local anesthetic ropivacaine was effective for postoperative analgesia (10). This study used the cross-over method to compare pain following the extraction of bilateral mandibular third molars (class II-B according to Pell and Gregory's classification) requiring bone removal under 0.75% ropivacaine or 2% lidocaine with 1:100,000 epinephrine. One of both anesthetics were administered by infiltration anesthesia, buccal nerve block, and inferior alveolar nerve block. Clinical studies that rely on self-reporting by patients often suffer from missing data. Therefore, the authors in this study made telephone calls to each patient every 30 minutes to enquire about the anesthetic effect. As a result, the data obtained were reliable. They found that the mean duration of anesthesia with 0.75% ropivacaine was 445.7±58 minutes (mean ± standard deviation), which was significantly longer than the 213.8±41 minutes with 2% lidocaine with 1:100,000 epinephrine. This is similar to the findings of Ogura *et al.* (11). Further, Amorim *et al.* found that the postoperative pain score on a visual analog scale (VAS) did not decrease significantly over 24 hours on administering 2% lidocaine with 1:100,000 epinephrine, whereas it decreased significantly within 8 hours on administering 0.75% ropivacaine. The total amount dosage and frequency of sodium dipyrone administered were also significantly lower when 0.75% ropivacaine was administered. Especially, at 72 hours, no patient took sodium dipyrone following 0.75% ropivacaine administration, unlike 20 patients who took following 2% lidocaine with 1:100,000 epinephrine administration. Therefore, the authors concluded that 0.75% ropivacaine exerts a preventive analgesic effect and diminishes pain following extraction of impacted third molars. I (KS) agree that 0.75% ropivacaine was more effective than 2% lidocaine with 1:100,000 epinephrine for post-extraction pain relief. However, it may not be possible

to state categorically whether this effect is the direct result of preventive analgesia as the authors claim.

Pain stimulation decreases the threshold of peripheral neurons and causes excitation of the central nervous system. Therefore, preventive analgesia is obtained by preventing pain input to the nervous system. On the other hand, long-acting anesthetics prolong the effect of postoperative analgesia, so that the dose of analgesics can be reduced. In addition, long duration of analgesia can help the patient recover oral function, including occlusion and swallowing, quickly, and there is a possibility that there is faster resolution of inflammation and pain owing to increased blood perfusion at the wound site. In short, it cannot be denied that long-acting anesthetics may decrease the amount of required analgesics through different reasons than preventive analgesia. Accordingly, the clinical study of preventive analgesia requires comparison of the postoperative pain levels of patients who undergo painless extractions and with those who undergo extractions under inadequate anesthesia. However, such research cannot be performed for ethical reasons.

This may be what underlies the difficulty in demonstrating preventive analgesia in a clinical setting. The authors have cited a study by Johansson *et al.*, which concluded that "Ropivacaine has a significant, dose-related pain-reducing effect in the immediate postoperative period but we could find no support for the theory that preoperative infiltration analgesia reduces long term pain" (12).

This study also discusses the vasoconstrictive action of 0.75% ropivacaine and the effect of adding epinephrine. The authors have cited past clinical studies according to which ropivacaine has vasoconstrictor properties (13,14) and epinephrine helps extend the duration time of vasodilating anesthetics like Lidocaine (15,16). On the other hand, Yamashiro *et al.* reported that 0.5% ropivacaine did not have a vasoconstrictive effect, and the addition of epinephrine tripled the concentration of ropivacaine in the maxillary tissue (17) in an experimental study on rats. Fujita *et al.* also reported that epinephrine addition had a greater effect on 0.5% ropivacaine than on 2% lidocaine in increasing the anesthetic concentration in the rat maxillary tissue (18). I believe that the cause for high postoperative bleeding following 0.75% ropivacaine administration in this study was that it did not have a vasoconstrictor effect. For these reasons, I consider that adding epinephrine to ropivacaine strengthens its anesthetic effect, provides long-lasting anesthesia, and decreases postoperative bleeding. Of course, as authors said that more clinical studies are needed about the use of ropivacaine with epinephrine in oral surgery and dentistry in general. However, I personally believe that ropivacaine with epinephrine would be a useful dental anesthetic solution.

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Footnote

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