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Efficacy of buprenorphine added to 2% lignocaine plus adrenaline 1:80,000 in providing postoperative analgesia after lower third molar surgery

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Abstract. A number of trials have examined the peripheral analgesic effect of opioids, known to have an anti-nociceptive effect at the central and/or spinal cord level. This study aimed to evaluate the efficacy of buprenorphine added to 2% lignocaine with adrenaline 1:80,000 in providing postoperative analgesia after lower third molar surgery. Sixty patients were randomized to three groups: group A received lignocaine 2% with adrenaline 1:80,000 for inferior alveolar nerve block (IANB), along with intramuscular (IM) injection of 1 ml saline; group B received buprenorphine mixed with lignocaine 2% with adrenaline 1:80,000 for IANB (0.01 mg buprenorphine/ml lignocaine with adrenaline), along with 1 ml saline IM; group C received lignocaine 2% with adrenaline 1:80,000 for IANB, along with 0.03 mg buprenorphine IM. Mean postoperative pain scores (visual analogue scale; when the patient first felt pain) were 6.0 for group A, 1.0 for group B, and 4.4 for group C. The mean duration of postoperative analgesia was 3.5 h in groups A and C and 12 h in group B. The mean number of postoperative analgesics consumed was 5.8 in groups A and C and 3.9 in group B. The addition of buprenorphine (0.03 mg) to 2% lignocaine with adrenaline 1:80,000 significantly reduced the severity of postoperative pain and prolonged the duration of analgesia, thereby decreasing the need for postoperative analgesics.

Key words: local analgesia; opioid analgesics; postoperative pain.

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Effective postoperative pain control is an essential component of the management of the surgical patient.[1] Traditionally, analgesics have been divided into centrally acting opioids (e.g. morphine) or peripherally acting non-steroidal anti-inflammatory drugs (NSAIDs; e.g. aspirin). Recent advances in pharmacology have challenged this strict distinction. Not only have local analgesic effects been recognized for opioids in peripheral tissue, but conversely NSAIDs have been

shown to act within the central nervous system.

Opioid analgesics are often the first line of treatment for many painful conditions and may offer advantages over NSAIDs; for example, they have no true 'ceiling dose' for analgesia and do not cause direct organ damage. Morphine is a μ-agonist opioid regarded as the gold standard of opioid analgesics used to relieve severe or agonizing pain. However, it produces a wide spectrum of unwanted effects, including respiratory depression, nausea, vomiting, dizziness, mental clouding, dysphoria, pruritus, constipation, urinary retention, hypotension, and increased pressure in the biliary tract. Therefore, an opioid with greater analgesic potential than morphine but with lesser adverse effects is desirable. Buprenorphine hydrochloride is an opioid receptor μ agonist and κ antagonist, having both analgesic and anti-hyperalgesic properties. It has rapid onset and a long duration of action. It has an anti-nociceptive potency approximately 25 to 50 times greater than that of morphine.[2] Adverse effects occur at a lower frequency than with morphine.

NSAIDs, which are used widely to treat pain and inflammation, are particularly useful in managing the pain associated with minimally invasive surgery. However, the associated side effects include peptic ulcer disease, gastrointestinal haemorrhage, renal dysfunction, altered liver function, and platelet dysfunction, which limit the use of these agents in some patients during the perioperative period.[1] Thus, there is a need for a drug that can provide good analgesia but which is without the associated adverse effects of the opioids and NSAIDs.

The recognition of opioid 'local analgesia' provides an opportunity to design new analgesics that produce no central side effects but retain potent analgesic actions. Peripheral opioid effects are not obvious in normal tissue but become so within minutes to hours after the start of inflammation; this is not a limiting factor, because most common, painful conditions are associated with inflammation. Small, systemically inactive doses of exogenous opioids administered in the vicinity of peripheral nerve terminals have beneficial analgesic effects. They have been used in brachial plexus block and have been reported to provide marked prolongation of analgesia.[3–6]

The aim of this prospective, randomized, double-blind clinical study was to evaluate the efficacy of buprenorphine added to 2% lignocaine with adrenaline 1:80,000 in providing postoperative analgesia after lower third molar surgery. The objectives of this study were to evaluate (1) the role of buprenorphine in the onset, duration, and depth of anaesthesia associated with lignocaine used for peripheral nerve block, (2) the severity of postoperative pain, (3) the duration of postoperative analgesia, (4) the decrease in number of rescue analgesics consumed by the patient, and (5) the adverse effects associated with buprenorphine when given with local anaesthetic used for peripheral nerve block.

Materials and methods

Sixty patients undergoing surgery for the removal of impacted mandibular third molars were selected on a random basis. Healthy patients aged 18–40 years without significant medical diseases or history of bleeding disorders, with impacted mandibular third molars, were included in the study.

The following patients were excluded from the study: those who were allergic or hypersensitive to any of the drugs used in the study; medically compromised patients with bleeding problems, diabetes, an immune-compromised status, or an osseous pathology affecting the surgical outcome and wound healing; patients with a history of asthma, neurological or psychiatric disease, or substance abuse; patients who had consumed analgesics ***with in*** the 6 hrs prior to surgical procedure; patients not returning the questionnaire given to them after the surgical procedure to assess their postoperative status; cases in which the inferior alveolar nerve block (IANB) failed.

A complete history was taken and a general physical and clinical examination was performed for all patients. This study was approved by the necessary institutional and ethics review board. All participants signed an informed consent form after which they were randomized by a dental nurse to one of the three study groups. The control group (group A) comprised patients who received lignocaine 2% with adrenaline 1:80,000 alone for IANB, along with intramuscular (IM) injection of 1 ml saline in the deltoid muscle of the arm. The first test group (group B) consisted of patients who received buprenorphine 0.01 mg per millilitre of lignocaine 2% with adrenaline 1:80,000 for IANB, along with IM injection of 1 ml saline in the deltoid muscle of the arm. The second test group (group C) consisted of patients who received lignocaine 2% with adrenaline 1:80,000 for IANB, along with IM injection of 0.03 mg buprenorphine in the deltoid muscle of the arm.

A slip system was used as the method of randomization, wherein three slips were made and labelled. The patient was asked to pick any one slip and they were allocated to the respective group accordingly.

A pulse oximeter was used during the procedure to record the patient's oxygen saturation, heart rate, and blood pressure.

Preparation of the solution for nerve block

One millilitre of 0.3 mg buprenorphine was added to 30 ml of lignocaine 2% with adrenaline 1:80,000. Thus each millilitre of this solution contained 0.01 mg of buprenorphine. This was done by a dental nurse, who then also dispensed the solution for nerve block during the procedure. Thus, the operator remained unaware of the solution used in the patient. The formulation used in this study was buprenorphine hydrochloride 0.3 mg (Buprigesic; Neon Laboratories Ltd, Mumbai, India); this was used for peripheral block as well as for IM injection.

Intramuscular injections in the deltoid muscle of the arm

All patients were given an IM injection into the deltoid muscle of the arm immediately following the administration of the local anaesthetic (LA). While, group A and group B patients received 1 ml of saline IM, group C patients received 1 ml of a reconstituted solution of 10 ml saline and 1 ml buprenorphine, such that the dose of buprenorphine received by the patient was 0.03 mg. The dental nurse prepared and gave the IM injection. The operator was unaware of the group allocations.

Administration of local anaesthesia

The classical direct IANB technique was used. All patients received a maximum of 3 ml of the solution (2 ml for IANB, 0.5 ml for lingual nerve block, and 0.5 ml for long buccal nerve block), irrespective of the group to which they belonged. Group A and group C patients received 3 ml of lignocaine 2% with adrenaline 1:80,000, while patients in group B received 3 ml of a reconstituted solution of a mixture of 30 ml lignocaine 2% with adrenaline 1:80,000 and 1 ml buprenorphine 0.3 mg (thus receiving a total dose of 0.03 mg buprenorphine).