Original Article

Use of 0.5% bupivacaine with buprenorphine in minor oral surgical procedures

ABSTRACT

Background: Minor oral surgical procedures are the most commonly performed procedures by oral and maxillofacial surgeons. Performance of painless surgical procedure is highly appreciated by the patients and is possible through the use of local anesthesia, conscious sedation or general anesthesia. Postoperative pain can also be controlled by the use of opioids, as opioid receptors exist in the peripheral nervous system and offers the possibility of providing postoperative analgesia in the surgical patient. The present study compares the efficacy of 0.5% bupivacaine versus 0.5% bupivacaine with 0.3 mg buprenorphine in minor oral surgical procedures.

Patients and Methods: The present study was conducted in 50 patients who required minor oral surgical procedures under local anesthesia. Two types of local anesthetic solutions were used- 0.5% bupivacaine with 1:200000 epinephrine in group I and a mixture of 39 ml of 0.5% bupivacaine with epinephrine 1:200000 and 1 ml of 300 µg buprenorphine (3 µg/kg)in group II. Intraoperative and postoperative evaluation was carried out for both the anesthetic solutions.

Results: The mean duration of postoperative analgesia in bupivacaine group (508.92 ± 63.30 minutes) was quite less than the buprenorphine combination group (1840.84 ± 819.51 minutes). The mean dose of postoperative analgesic medication in bupivacaine group (1.64 ± 0.99 tablets) was higher than buprenorphine combination group (0.80 ± 1.08 tablets). There was no significant difference between the two groups regarding the onset of action of the anesthetic effect and duration of anesthesia.

Conclusion: Buprenorphine can be used in combination with bupivacaine for patients undergoing minor oral surgical procedures to provide postoperative analgesia for a longer duration.

Keywords: Bupivacaine, buprenorphine, minor oral surgical procedures

INTRODUCTION

Local anesthetic agents are the mainstay of perioperative pain control for most office-based oral surgical procedures. Amide types of local anesthetics (bupivacaine, etidocaine, lidocaine, mepivacaine, prilocaine, and articaine) with a moderate-to-long duration of action are commonly used for these surgical procedures.[1]

Bupivacaine hydrochloride, introduced in 1963, is a long-acting amide type of local anesthetic. It is a powerful anesthetic with an intermediate onset of action (2–5 min), allowing a slow return to normal sensation (180–600 min).[2] It provides additional analgesia time, known as residual analgesia, and minimizes the duration of postoperative pain, facilitating postoperative care, and maintenance of proper oral hygiene.[3]

Infection if present alters the ability of local anesthetic to achieve adequate pain control during surgery as the low pH

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of the inflamed tissue leads to quick dissociation of local anesthetic to cation form, which is not able to penetrate the phospholipid membrane of the neuronal cells. Locally injected opioids may act synergistically with local anesthetics in inflamed tissues and increase the perioperative analgesic effect.[4]

Buprenorphine is a semi-synthetic, oripavine alkaloid derived from thebaine. It is a long-acting, lipid-soluble, mixed agonist-antagonist opioid analgesic which was first synthesized in 1966.[5] The low abuse liability of the drug in humans soon turned it into a widely used therapeutic agent in patients with opioid dependence. The principal clinical application of buprenorphine is as an analgesic for moderate-to-severe pain in perioperative setting.[6] The analgesic effect of buprenorphine appears to depend on the integrity of descending fibers from the rostral ventromedial medulla. Residual analgesic effects of opioids after inactivation of descending fibers may be caused by peripheral effects in the presence of inflammation.[7] Buprenorphine is shown to be fully efficacious with an antinociceptive potency 20-70 times higher than morphine. It binds to mu, kappa, and delta opioid receptors and dissociates slowly from these receptors. Buprenorphine acts as a partial mu opioid agonist and a kappa opioid antagonist.[8] The parenteral formulation of buprenorphine has an onset time of 5-15 min, and duration of action is about 8 h after administration. It is metabolized by the gut and liver.

The various advantages associated with the use of buprenorphine are that it has a longer duration of analgesic action, low addiction propensity, and a high therapeutic index. The adverse effects associated with it include sedation, nausea, itching, constipation, addiction in higher doses, confusion, hallucinations, dry mouth, blurred vision, and respiratory depression with the overdose of drug.[6,7]

The purpose of the study was to compare the efficacy of 0.5% bupivacaine versus 0.5% bupivacaine with buprenorphine in providing prolonged postoperative analgesia during various minor oral surgical procedures.

PATIENTS AND METHODS

Fifty healthy adult patients who reported to the department of oral and maxillofacial surgery requiring minor oral surgical procedures were included in this study. Various minor surgical procedures included incision and drainage of abscess, removal of impacted third molars, apicoectomy, neurectomy, surgical extraction of teeth, cyst enucleation, and fracture reduction and fixation under local anesthesia. Diagnosis was made on the basis of history, clinical examination, and radiological examination. Patients were informed about the surgical procedure, postsurgical recommendations, and possible complications. Informed consent was obtained from each patient. Exclusion criteria included patients with a history of uncontrolled medical illness, sensitivity to local anesthesia, tolerance or addiction to analgesic drugs, pregnancy, bleeding disorders, chronic obstructive pulmonary disease, neurologic, psychiatric illness, or positive drug abuse history. The study protocol and informed consent form was approved by the Institutional Ethical Committee.

Treatment groups

Patients were assigned to one of the two equal groups by randomization method using table of random numbers. Patients in Group I (25 patients) received various intraoral nerve blocks as indicated using 0.5% bupivacaine with 1:200,000 epinephrine, whereas patients in Group II (25 patients) received the same blocks using the mixture of 39 ml of 0.5% bupivacaine with 1:200,000 epinephrine and 1 ml of 300 microgram buprenorphine (3 μg/kg). In addition, local infiltration was given in both the groups wherever needed to achieve hemostasis of the site. Analgesics were prescribed postoperatively only when the patient began to complaint of pain. The prescribed analgesic was tablet ketorol 10 mg (ketorolac 10 mg - Dr. Reddy's Laboratories Limited). Patients were asked to note down the number of tablets required, if any, to relieve pain.

Assessment

It included evaluation of following parameters in both the groups intraoperatively and postoperatively:

1. Total volume of anesthetic solution used during the surgery (in ml)
2. Onset of action of anesthetic agent: The onset of anesthesia was determined by evaluating the subjective and objective symptoms of anesthesia of the respective nerve block used
3. Duration of surgery after anesthetic administration (in minutes): The duration of surgery corresponded to the period between the first incision and the last suture
4. Duration of anesthesia (in minutes): The duration of anesthesia was determined as the time from onset of anesthesia to the time when symptoms of anesthesia began to wear off
5. Duration of postoperative analgesia (in minutes): The duration of postoperative analgesia was taken as the time from the end of surgery to the time for the need of first analgesic medication. The total amount of analgesic medication ingested during the postoperative period, and the percentage of patients who required medication in each group was also evaluated
6. Efficacy of postoperative analgesia: The efficacy of analgesia was recorded with the aid of a 100 mm-length visual analog scale (VAS) with the markings between:

a. 1–25: Mild pain
b. 26–50: Moderate pain
c. 51–75: Intense pain
d. 76–100: Unbearable pain
   - Each patient scored pain intensity every hourly for the first 10 h and then again at 24, 36, and 48 h.

7. Patients were observed for side effects such as sedation, pruritus, nausea, vomiting, and respiratory depression.

Statistical analysis

The data obtained were subjected to statistical analysis and expressed as mean ± standard deviation. Unpaired *t*-test was used to analyze the data for the mean volume of anesthetic solution, onset and duration of anesthesia, postoperative analgesia, and duration of surgery for both the groups. Data for the percentage of patients taking postoperative analgesics were analyzed using nonparametric Chi-square test. Mann–Whitney test was used for the evaluation of pain with VAS because the data were not normally distributed, $P < 0.01$ was considered statistically significant.

RESULTS

Out of total 50 patients selected for the study, there were 29 (58%) male and 21 (42%) female [Figure 1]. The mean age of patients was 27.60 years in bupivacaine group and 27.50 years in buprenorphine combination with bupivacaine group.

Patients were divided into two groups and the surgical procedures included surgical removal of impacted mandibular third molars, incision and drainage of space infections, enucleation of cysts, dentoalveolar fractures, isolated mandibular fractures, maxillary fractures, elective implant removal, and excision of tumors [Figure 2].

In both groups, the minimum volume of anesthetic solution used was 4 ml. However, the mean volume of bupivacaine solution including the amount needed for infiltration/reanesthesia was slightly higher (4.15 ± 0.52 ml) than the mean volume of buprenorphine combination with bupivacaine solution (4.12 ± 0.60 ml). The difference in the mean volume of both the solutions used was found to be statistically nonsignificant ($P = 0.84$).

The mean subjective onset of action in bupivacaine group (3.00 ± 1.08 min) was slightly longer than buprenorphine combination group (2.92 ± 1.03 min) whereas, on pinprick test, reverse was the case with the mean of 7.40 ± 1.93 min in buprenorphine combination group and 7.28 ± 1.59 min in bupivacaine group [Table 1]. Statistically, no significant difference was observed between both groups regarding subjective ($P = 0.79$) and objective onset of action ($P = 0.81$).

Similarly, there was no significant difference in the duration of surgical procedure ($P = 0.76$) and duration of anesthesia with respect to initial recovery from anesthesia and complete recovery of sensation in both groups ($P = 0.32$, $P = 0.63$, respectively). However, the mean duration of postoperative analgesia in bupivacaine group (508.92 ± 63.30 min) was observed to be quite less than buprenorphine combination group (1840.84 ± 819.51 min), and value was found to be highly significant statistically ($P < 0.001$) [Table 2].

On comparing the total amount of analgesic medication ingested during the postoperative period, the mean dose of analgesic medication in bupivacaine group (1.64 ± 0.99 tablets) was observed to be higher than buprenorphine combination group (0.80 ± 1.08 tablets). The difference between both the anesthetic solutions regarding number of analgesic tablets was found to be statistically significant ($P = 0.006$) [Table 3].

The percentage of patients who had taken analgesic medication in the early postoperative period (1, 2, 3, 4, 5, 6, 7, 8, 9, and 10 h) and in the later postoperative period (12, 24, 36 and 48 h) was compared in both the groups, and it revealed that the patients in buprenorphine combination group had significantly less pain during both periods [Figure 3]. At the end of 10 h, all patients (100%) in buprenorphine combination group were pain free, as compared to only 4%

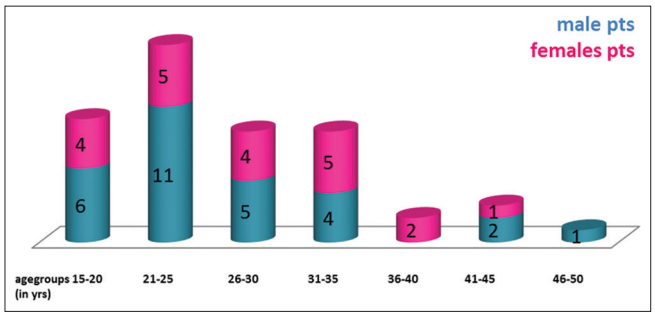

Figure 1: Demographic data

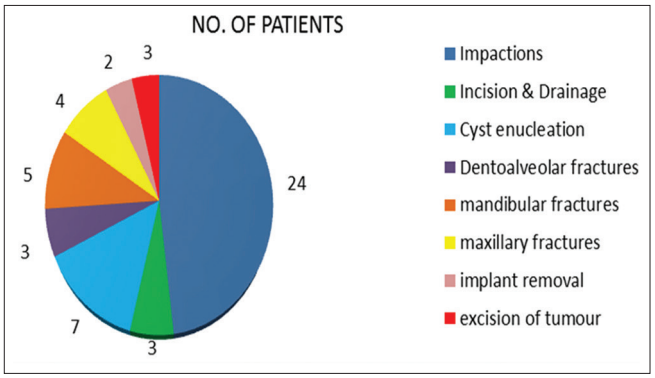

Figure 2: Various minor oral surgical procedures done

Table 1: Evaluation of onset of action

Parameters	Bupivacaine group ($n=25$)			Buprenorphine combination group ($n=25$)			*P*
	Mean±SD (min)	SEM	Range (min)	Mean±SD (min)	SEM	Range (min)	
Numbness of lip and tongue	3.00±1.08	0.21	1-6	2.92±1.03	0.20	1-5	0.79 (NS)
Pinprick	7.28±1.59	0.31	4-10	7.40±1.93	0.38	3-10	0.81 (NS)

SD: Standard deviation, *n*: Number of patients, NS: Not significant, SEM: Standard error mean

Table 2: Evaluation of duration of anesthesia, postoperative analgesia, and duration of surgery

Parameters	Bupivacaine group ($n=25$)			Buprenorphine combination group ($n=25$)			*P*
	Mean±SD	SEM	Range	Mean±SD	SEM	Range	
Duration of anesthesia (min)							
Initial recovery of anesthesia	284.92±50.28	10.05	190-375	301.60±66.47	13.29	200-390	0.32 (NS)
Final recovery from anesthesia	526.84±101.1	20.22	371-788	540.80±103.78	20.75	314-717	0.63 (NS)
Duration of postoperative analgesia (min)	508.92±63.30	12.66	400-705	1840.84±819.5	163.90	606-2880	<0.001***
Duration of surgery (min)	32.20±15.50	3.10	11-68	33.68±18.91	3.78	9-74	0.76 (NS)

***$P<0.001$ (highly significant). SD: Standard deviation, *n*: Number of patients, NS: Not Significant, SEM: Standard error mean

Table 3: Evaluation of analgesic medication

Parameters	Bupivacaine group ($n=25$)			Buprenorphine combination group ($n=25$)			*P*
	Mean±SD	SEM	Range	Mean±SD	SEM	Range	
Total amount of analgesic medication (number of tablets)	1.64±0.99	0.19	1-4	0.80±1.08	0.21	0-3	0.006**

**$P<0.01$ (significant at 1% significance level). SD: Standard deviation, *n*: Number of patients, SEM: Standard error mean

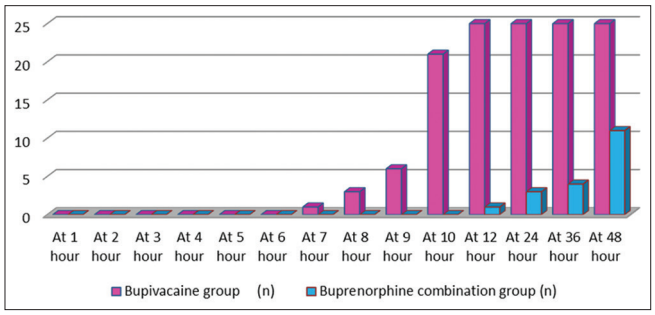

Figure 3: Patients who had taken analgesic medication

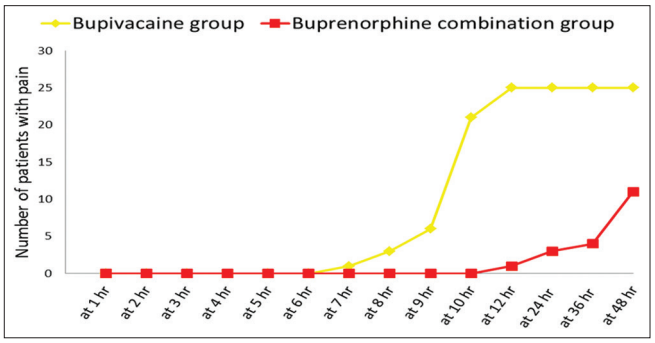

Figure 4: Evaluation of pain using visual analog scale

of patients who were absolutely pain free in bupivacaine group. In this group, 12% of patients had mild pain but did not take analgesic medication. Only 84% of patients took analgesic medication till the 10th h evaluation. However, at 12, 24, and 36 h, 4%, 12%, and 16% of patients, respectively, in buprenorphine combination group had taken analgesic medication as compared to 100% of patients in bupivacaine group at all-time intervals. At the 48th h, 20% of patients were still pain free in buprenorphine combination group as compared to no pain-free patient in bupivacaine group.

The difference between number of analgesic tablets taken in both groups was statistically highly significant at the 10th, 12th, 24th, 36th, and 48th h ($P < 0.001$) [Table 4].

The efficacy of postoperative analgesia was recorded with the help of 100 mm-length VAS in both the groups [Figure 4]. Till the 5th postoperative hour, the *P* value was found to be statistically insignificant as all the patients in buprenorphine combination group had no pain and only three patients in bupivacaine group had very mild pain. Difference in median postoperative pain score between both anesthetic solutions was found to be statistically significant at the 6th and 10th h ($P = 0.001$). However, it was observed to be statistically highly significant from 7th h to 9th h ($P < 0.001$). As all the patients in the bupivacaine group had taken analgesic medication by the 12th h, they were excluded from further statistical analysis [Table 5].

None of the patients in either group reported opioid-related side effects such as nausea, vomiting, pruritus, or any evidence of respiratory depression during intraoperative and postoperative assessment.

DISCUSSION

Pain may be described as an unpleasant sensory and emotional experience associated with actual or potential

Table 4: Percentage of patients who had taken analgesic medication

Postoperative follow up period	Bupivacaine group (*n*), *n* (%)	Buprenorphine combination group (*n*), *n* (%)	χ^2	*P*
At 1 h	-	-	-	-
At 2 h	-	-	-	-
At 3 h	-	-	-	-
At 4 h	-	-	-	-
At 5 h	-	-	-	-
At 6 h	-	-	-	-
At 7 h	1 (4)	0	1.02	0.31 (NS)
At 8 h	3 (12)	0	3.19	0.07 (NS)
At 9 h	6 (24)	0	6.81	0.09 (NS)
At 10 h	21 (84)	0	36.20	<0.001***
At 12 h	25 (100)	1 (4)	46.15	<0.001***
At 24 h	25 (100)	3 (12)	39.28	<0.001***
At 36 h	25 (100)	4 (16)	36.20	<0.001***
At 48 h	25 (100)	11 (44)	19.44	<0.001***

***$P<0.001$: Highly significant. *n*: Number of patients, NS: Not significant;

Table 5: Evaluation of pain using visual analog scale

Parameters	*n*	Bupivacaine group			*n*	Buprenorphine combination group			*P*
		Median	Mean rank	Range		Median	Mean rank	Range	
At 1 h	0	0.00	25.50	0-0	0	0.00	25.50	0-0	1.00 (NS)
At 2 h	0	0.00	25.50	0-0	0	0.00	25.50	0-0	1.00 (NS)
At 3 h	0	0.00	26.00	0-10	0	0.00	25.00	0-0	0.31 (NS)
At 4 h	0	0.00	26.00	0-10	0	0.00	25.00	0-0	0.31 (NS)
At 5 h	0	0.00	27.00	0-25	0	0.00	24.00	0-0	0.07 (NS)
At 6 h	0	5.00	33.50	0-50	0	0.00	17.50	0-0	0.001**
At 7 h	1	25.00	36.81	0-65	0	0.00	13.66	0-10	<0.001***
At 8 h	3	37.50	36.32	0-75	0	0.00	13.16	0-27	<0.001***
At 9 h	6	65.00	34.95	0-75	0	0.00	13.04	0-35	<0.001***
At 10 h	21	67.50	27.50	0-75	0	0.00	13.00	0-60	0.001**
At 12 h	25	-	0.00	-	1	0.00	12.50	0-70	-
At 24 h	25	-	0.00	-	3	10.00	11.50	0-60	-
At 36 h	25	-	0.00	-	4	10.00	11.00	0-75	-
At 48 h	25	-	0.00	-	11	0.00	7.50	0-20	-

**$P<0.01$ (Significant at 1% significance level), ***$P<0.001$ (highly significant), *n* represents number of patients who had taken analgesic medication postoperatively. NS: Not significant

tissue damage. Buprenorphine has been used for the treatment of acute and chronic pain as a supplement to anesthesia for behavior and psychiatric disorders and as a maintenance medication for heroin dependence.[6,7] The analgesic effect of buprenorphine appears to depend on the integrity of descending fibers from the rostral ventromedial medulla. Prolonged duration of analgesia is due to the fact that buprenorphine dissociates very slowly from opioid receptors. The postoperative analgesic effects of buprenorphine added to local anesthetic have been discussed by various authors.[7-10]

Being a partial mu opioid agonist, buprenorphine has a wider safety profile as compared to full mu agonists. Further, the slow dissociation of buprenorphine from the receptor may result in fewer signs and symptoms of opioid withdrawal upon termination of buprenorphine therapy than those which occur with full mu opioid agonists such as morphine, heroin, and methadone. Antagonist effects at the kappa receptors are associated with limited spinal analgesia, dysphoria, and psychomimetic effects.[6] Buprenorphine can be used by various routes in human beings such as epidural, intravenous, intramuscular, sublingual, transdermal, delivery routes[6-8] and for intraoral nerve blocks.[8]

The pH of the tissue and pKa of drug are the most important factors which affect the time of onset of anesthesia. The pKa defines the pH at which the ionized and nonionized forms of a drug are in complete equilibrium, that is, half of the drug is ionized. Only the nonionized form of the local anesthetic can diffuse across lipid nerve sheath and cell membrane. pKa also reflects the proportion of local anesthetic that is in a diffusible nonionized state and therefore contributes greatly to the rate of onset of anesthesia. The pKa values

of commonly used local anesthetics are greater than the normal tissue pH (approximately 7.4) which means the drugs exist predominantly in the ionized form after injection. At normal tissue pH, the proportion of nonionized form of bupivacaine is 20%; this contributes in part to slightly slower onset of anesthesia with bupivacaine, particularly for nerve block anesthesia.[2,11,12] In the present study, the mean value for time of onset as referred to lip and tongue numbness and also on pinprick test in bupivacaine group was 3.00 ± 1.08 and 7.28 ± 1.59 min, respectively, as compared to 2.92 ± 1.03 min and 7.40 ± 1.93 min, respectively, in buprenorphine combination group. Contrary to our results, Brkovic *et al*.[13] found the mean time of onset as referred to lower lip numbness as 8.7 ± 2.2 min and 7.4 ± 1.4 min on pinprick test while using 0.5% bupivacaine (2 ml) for the lower third molar surgery. Swarnkar *et al*.[14] reported the onset time of sensory block (with intravenous regional anesthesia) when 0.3 mg buprenorphine was added to the local anesthetic as 5.0 ± 1.0 min and the onset time of sensory block as 4.0 ± 0.4 min when 0.3 mg buprenorphine was given intramuscularly. Sarkar *et al*.[15] reported the onset time of sensory block as 3.28 min (supraclavicular block) when 1 ml (0.3 mg) buprenorphine was added to the mixture of local anesthetics. Our results are in agreement with those of Trullenque-Eriksson and Guisado-Moya[3] who found the mean onset of time for inferior alveolar nerve block as 3.68 ± 3.11 min and for buccal nerve as 1.95 ± 1.25 min while using 0.5% bupivacaine with 1:200,000 epinephrine for surgical extraction of mandibular third molars. Duration of the effect of an anesthetic is proportional to its degree of protein binding. Those agents who have a high affinity for the protein component of a nerve are less liable to diffuse from the injection site and be absorbed into the systemic circulation. Bupivacaine's long duration of action is largely due to this characteristic. Bupivacaine has one of the greatest protein binding values out of all the amide local anesthetics. The reported protein binding value for bupivacaine is 95%. However, the duration of the effect of the local anesthetic is also dependent on the injection site and the concentration of vasoconstrictor present in the anesthetic solution.[2,11,12] In the present study, there was no statistically significant difference in the mean duration of anesthetic effect of 0.5% bupivacaine with epinephrine 1:200,000 (526.84 ± 101.13 min) and buprenorphine combination group (540.80 ± 103.78 min). Our results are in agreement with Brkovic *et al*.[13] who reported that duration of anesthesia was slightly longer with 0.5% bupivacaine (688 ± 85 min and 550 ± 48 min) as compared to 0.75% ropivacaine group (582 ± 67 min and 450 ± 73 min) with reference to lower lip numbness and pinprick test, respectively.

In contrast to the present study, Sarkar *et al*.[15] reported the total duration of sensory block and motor block when 1 ml (0.3 mg) buprenorphine was added to the mixture of local anesthetics for supraclavicular block as 261.84 ± 53.30 min and 328.32 ± 47.94 min, respectively, which was less than the present study. Trullenque-Eriksson and Guisado-Moya[3] reported the duration of soft-tissue anesthesia being 8.20 ± 4.54 h in case of 0.5% bupivacaine with 1:200000 epinephrine group. Our results are also supported by Sancho-Puchades *et al*.[16] who compared 4% articaine and 0.5% bupivacaine both with epinephrine 1:200000 and reported that mean duration of soft-tissue anesthesia with respect to the final lip recovery (621.2 ± 148.4 min) was longer than final tongue recovery (512.1 ± 127.3 min). Singam *et al*.[17] reported the total duration of sensory block and motor block when 2 ml (0.3 mg) buprenorphine was added to the local anesthetic and then used for supraclavicular block as 647.83 ± 55.70 min and 306.33 ± 20.12 min, respectively, which is quite close to the findings of the present study.

Postoperative pain control has been the subject of continuous research in the field of oral and maxillofacial surgery since pain can interfere with patient's quality of life. Surgical trauma elicits a variety of tissue responses producing and releasing biochemical mediators involved in the pain process.[18] Several authors have studied the various methods to control pain, such as the use of long-acting local anesthetics to decrease analgesic intake, the preoperative prescription of steroidal anti-inflammatory drugs for decreasing edema, pain and the postoperative use of soft-tissue lasers for better healing, and less postoperative pain and inflammation.[19] In the present study, duration of postoperative analgesia in bupivacaine group was 508.92 ± 63.30 min and in buprenorphine combination group being 1840.84 ± 819.51 min. Opioids exert their analgesic effect by acting exclusively in the central nervous system. Various mechanisms are proposed for activation of opioid receptors on peripheral neurons.

a. Opioids increase potassium current and decrease calcium current in the cell bodies of sensory neurons. This inhibits the neuronal firing and transmitter release as well as the calcium-dependent release of excitatory pro-inflammatory compounds (e.g., substance P) which contributes to their analgesic and anti-inflammatory actions
b. Opioid antinociceptive effect is particularly prominent in inflamed tissue
    i. Inflammation disrupts the perineurium (normally an impermeable membrane) and facilitates the passage of corticotropin-releasing hormones, interleukin 1B, and other cytokines. These substances apparently stimulate the release of opioid peptides from

immune cells which activate opioid receptors on the sensory nerve endings leading to antinociception

ii. Inflammation also enhances the peripherally directed axonal transport of opioid receptors (dorsal root ganglia → peripheral) which leads to receptor upregulation (increase in their number in peripheral nerve terminals). Furthermore, the previously inactive opioid receptors become active in an inflamed tissue enhancing the analgesic potential of

iii. Opioids.

Prolonged duration of analgesia is due to the fact that buprenorphine dissociates very slowly from opioid receptors.[8,20-22] Our results are supported by Nespeca,[23] Bouloux and Punnia Moorthy,[24] and Modi *et al*.[8] who found duration of postoperative analgesia in 0.5% bupivacaine with 1:200000 epinephrine groups as 449 ± 19.25 min, 480 min, and 500.4 ± 6.6 min, respectively, in their studies. Viel *et al*.[9] reported duration of postoperative analgesia when 0.3 mg buprenorphine was added to 0.5% bupivacaine in brachial plexus block as 2103 ± 117 min. Our results are supported by Modi *et al*.[8] who found duration of postoperative analgesia in Group II patients (0.3 mg of buprenorphine combined with 0.5% bupivacaine with epinephrine 1:200,000) as 1690.8 ± 61.2 min. The authors stated that the addition of buprenorphine to the local anesthetic mixture prolonged the duration of postoperative analgesia up to three times provided by the local anesthetics alone.

Tissue injury associated with surgical trauma directly and indirectly leads to the activation of nociceptors with increased expression of pro-inflammatory cytokines and induction of cyclooxygenase-2 leading to peripheral and central sensitization with subsequent hyperalgesia. Prostaglandin E_2 is an abundant eicosanoid released after surgical trauma and has been associated with inflammation and pain. The synthesis of prostaglandin is suppressed by a number of anti-inflammatory agents including the nonsteroidal anti-inflammatory drugs.[25,26] In the present study, the mean dose of postoperative analgesic medication tablet ketorol DT 10 mg (ketorolac 10 mg Dr. Reddy's) in bupivacaine group ([1.64 ± 0.99 tablets] 16.4 ± 9.9 mg) was higher than buprenorphine combination group ([0.80 ± 1.08 tablets] 8 ± 10.8 mg). Trieger and Gillen[25] reported that patients receiving 0.5% bupivacaine with epinephrine 1:200000 required only 2.3 doses of codeine phosphate (30 mg) as postoperative analgesics. Our results are supported by Crout *et al*.[26] who found that only 1.4 ± 1.0 tablets of postoperative analgesic medication (325 mg acetaminophen with codeine 30 mg) were required in 0.5% bupivacaine with epinephrine 1:200000 group. Contrary to our results, Brkovic *et al*.[13] reported that there was no requirement of analgesic tablet in 0.5% bupivacaine group patients. Swarnkar *et al*.[14] found that 56 ± 9 mg of postoperative analgesic medication (diclofenac 1 mg/kg) was consumed when 0.3 mg of buprenorphine was added to local anesthetic for intravenous regional anesthesia. Analgesic dose consumption was higher (120 ± 24 mg) when 0.3 mg of buprenorphine was given intramuscularly as compared to intravenous route. Mehta *et al*.[21] reported that total dose of postoperative analgesic medication (tramadol 50 mg) consumed was 12.5 ± 5.38 mg when 2 μg/kg of buprenorphine was added to local anesthetic for wound infiltration.

In the present study, VAS was used for assessment of postoperative pain. At the end of 10th h, all patients (100%) in buprenorphine combination group were pain free, as compared to only 4% pain-free patients in bupivacaine group. At the 48th h, 20% of patients were still pain free in buprenorphine combination group as compared to none in the bupivacaine group. Viel *et al*.[9] compared the effectiveness of both buprenorphine and morphine when used in combination with local anesthetic (5% bupivacaine) in brachial plexus block for postoperative pain relief. The authors reported that 12 h postanesthesia, all patients (100%) had satisfactory or tolerable anesthesia in buprenorphine group as compared to 80% of patients in morphine group. At the 48th h, 5% of patients were still pain free in buprenorphine combination group as compared to no pain-free patient in morphine combination group. Candido *et al*.[10] also studied that the addition of buprenorphine to local anesthetic used for brachial plexus block provided long-lasting postoperative analgesia with complete analgesia persisting 30 h beyond the duration (6 h) provided by local anesthetic alone in 75% of patients. In their study, at the 48th h evaluation, 10% of patients were pain free in buprenorphine combination group as compared to no pain-free patient in local anesthetic group. Their findings are in agreement with the present study and with the findings of Modi *et al*.[8] in which also postoperatively at the 48th h evaluation, 20% of patients of buprenorphine combination group were pain free as compared to no pain-free patient in bupivacaine group.

CONCLUSION

Buprenorphine in combination with 0.5% bupivacaine group in comparison to 0.5% bupivacaine group alone provided a longer duration of postoperative analgesia and markedly decreased the need for analgesic medication in postoperative period. Overall, buprenorphine is a highly effective analgesic for the treatment of moderate-to-severe pain. It has a unique

pharmacological and physiochemical profile allowing for relatively safe use and flexibility with regard to dosage and dosage forms. Thus, buprenorphine can be used in combination with bupivacaine for patients undergoing minor oral surgical procedures to provide postoperative analgesia for a longer duration, but it should be used cautiously in individuals with a past or current history of substance abuse or dependence, as it produces opioid-like subjective and physiologic effects dependent on the dose and the route of administration.

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Conflicts of interest

The authors wish to state that this paper does not have any financial and personal relationships with other people or organizations that could inappropriately influence (bias) their work.

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