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Original Research Article

Comparative analysis of post-operative analgesic requirements in patients undergoing minor oral surgery using buprenorphine with lignocaine versus lignocaine: a clinical study

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ABSTRACT

Background: We aimed to inspect the post -operative analgesic requirement in patient undergoing minor oral surgery using buprenorphine versus lignocaine and lignocaine alone. Minor oral surgeries are followed by inflammatory reaction characterized by pain, mild swelling and discomfort. Opioid analgesics have an advantage over non-steroidal anti-inflammatory drugs (NSAIDs) as they do not cause organ damage. Buprenorphine has an antinociceptive potency greater than that of morphine. Hence, in this study, buprenorphine was added to lignocaine in relieving postoperative pain after minor oral surgery.
Methods: A total of 100 patients requiring minor oral surgery were included in the study. The patients were randomized by a third party and allocated to one of the two study groups. Hence a total of 50 patients in each group were selected for study, during a period of 24 months. 1 ml of buprenorphine hydrochloride injection I.P which contains an equivalent of 0.3 mg buprenorphine was withdrawn into a syringe and injected into a 30 ml vial of 2% lignocaine with adrenaline 1:200000.
Results: The pain was found to be statistically significant at 2-hour, 24 hour and 36 hours postoperatively, thereafter the difference in NRS values between the solutions was not significant. Hence, the analgesic effect of solution A (buprenorphine) was effective at 2-hour, 24 hour and 36 hours postoperatively.
Conclusions: Our study indicate that addition of 0.3 mg of buprenorphine to local anesthetic solution provides efficient post-operative analgesia and reduces patient's discomfort.

Keywords: Buprinorphine, Lignocaine, Minor oral surgery

INTRODUCTION

Pain is an unpleasant emotional experience usually initiated by a noxious stimulus and transmitted over a specialized neural network to the central nervous system where it is interpreted as such. After noxious stimuli prostaglandins are released from cell membrane through cyclo-oxygenase pathway and they mediate inflammation and inflammatory induced pain. In most cases pain reaction threshold is lowered by fear, apprehension, fatigue and emotional stress. Centuries ago, opium was determined to be “god's own medicine” which produced definite analgesic effect and also eliminated fear, anxiety and suffering.[1]

Normally, minor oral surgeries are followed by inflammatory reaction characterized by pain, mild swelling and discomfort. Pain control in dentistry helps to reduce the fear and anxiety and improves dental treatment. The management of postoperative pain after surgery can be achieved by use of long-acting local anaesthetic agent, ice therapy, opioids and non-steroidal anti-inflammatory drugs (NSAIDs). The presence of opioid receptors in peripheral nervous system offers the possibility of providing post-operative analgesia with the help of opioids in ambulatory surgical patients. Over the past decades many investigators have studied this approach and have compared the efficacy of various opioids added to the local anesthetics injected into inflamed dental tissues and also in brachial plexus blocks.[2-5]

Buprenorphine, first synthesized in 1966, is a semisynthetic, oripavine alkaloid derived from the baine and binds to all three receptors. Buprenorphine is highly lipophilic and is better diffused into the perineurium. It produces longer effect of analgesia compared to morphine and sufentanil. It is at least 30 to 50 times more potent than morphine sulphate and has substantially longer duration of action. Few studies have been conducted in past which prove the efficacy of buprenorphine in bupivacaine as a post-operative analgesic in minor oral surgery. Bupivacaine has longer duration of action itself so it is difficult to analyze whether post-operative analgesic effect in minor oral surgical procedure is due to the effect of bupivacaine or buprenorphine. Kumar and colleagues compared the onset, quality and duration of analgesia produced by lignocaine hydrochloride 1:80000 adrenaline with buprenorphine versus lignocaine hydrochloride with 1:80000 adrenaline in minor oral surgical procedures e.g. cyst enucleation and alveoloplasty.[6,7]

Aim

The aim of this study was compared to analysis of post-operative analgesic requirement in patient undergoing minor oral surgery using buprenorphine versus 2% lignocaine with 1:200000 adrenaline and 2% lignocaine with 1:200000 adrenaline.

Objectives

Objectives of the study were: to evaluate the onset of action of anesthesia of 2% lignocaine with 1:200000 adrenaline with buprenorphine as compared to 2% lignocaine with 1:200000 adrenaline; to measure the duration of anesthesia of both solutions; and to evaluate the duration of post extraction analgesia and requirement of medication in patients injected with 2% lignocaine with 1:200000 adrenaline with buprenorphine as compared to 2% lignocaine with 1:200000 adrenaline.

METHODS

This study was conducted in the department of oral and maxillofacial surgery at Rajasthan Dental College and Hospital, Jaipur. The study was undertaken for a period of two years i.e. from October 2018 till September 2020. The sample size was taken 100 (n=100) which included male and female patients (male=48, female=52).

The protocol for the study was approved by the ethical committee of the institutional review board and written informed consent was obtained from every patient. 100 patients requiring minor oral surgery were included in the study. The patients were randomized by a third party and allocated to one of the two study groups. This allowed the patients and the operators to remain unaware of the group allocations.

Inclusion criteria

Patients in the age group between 22-50 years and having no systemic illness, requiring minor surgical procedures and who were willing to take part in study were included.

Patients who had not taken any pre-operative medications before the planned minor surgery were included in this study.

Patients with ASA grade I and II were also included.

Exclusion criteria

Patients who were allergic to any of the components of local anesthetic solutions, buprenorphine or any other medications prescribed in the study; presence of acute infection or swelling; pregnant patients; medically compromised patients with ASA grade III, IV and V; patients who were unable to provide informed consent to the maxillofacial surgeon at the time of procedure; and any patient requiring supplementary local anaesthetic injection during procedure were included.

Armamentarium used in this study

Drugs and instruments used during the course of the study are mentioned as: stopwatch, solution A or solution B for injection, 3 ml 26-gauge syringe and needle, extraction forceps, elevator set, suturing material, and minor surgery kit.

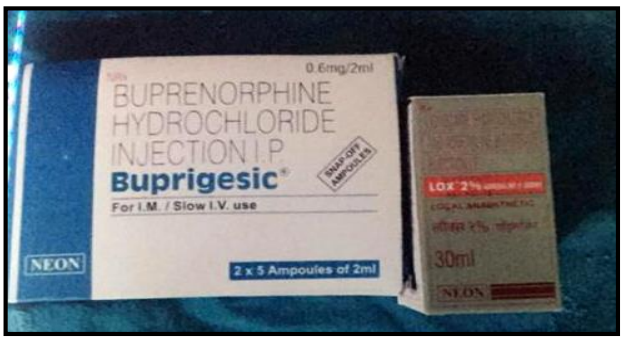

Figure 1: Buprenorphine and local anesthetic solution.

Sample size

Considering the mean and SD of duration of analgesia as per NRS score at the end of 72 hour is 3.3±2.7 at allowable error±1, the calculated sample size n was 120.[5]

Using statistical formula, where N is the number of patients, σ is sigma, and L is duration of time.

$$N = \frac{4\sigma^2}{L^2}$$

Study design

Double blinding of the operator and patient was achieved by appointing a custodian who was not to be a participant in this study in any way. The custodian prepared and dispensed the solution to the operator allocating the patient into two groups, A and B randomly, He maintained a record of the patient details and the solution dispensed in custodian record.

One of the solution A had 2% lignocaine hydrochloride with 1:200000 adrenaline bitartrate along with buprinorphine 0.3 mg and solution B had 2% lignocaine hydrochloride with 1:200000 adrenaline bitartrate for intra oral nerve block to achieve local anesthesia.

Following parameters were recorded in patient performa and assessed: onset of action of anesthesia, duration of surgery, duration of anaesthesia, duration of analgesia, and numeric pain rating scale (NPRS).

Pain assessment

After the surgical procedure, patients were given a self-analysis form to evaluate the degree of post-surgical pain. They were instructed to note the intensity of pain and the number of post-operative analgesics consumed during the next 72 hours, at intervals of 2, 4, 6, 12, 24, 36 and 48 hours, and 72 hours.

Patients daily rating of discomfort was done on a 3-point, numeric rating scale for pain; (NRS scale). Patients were instructed to document the number of rescue medication consumed and the timing of first analgesic intake during the study period. 1 ml of solution was used for every nerve block given in this study.[8]

Data analysis

Results were calculated using the mean value and standard deviation for each of the parameters considered and checked for statistical significance using the following: descriptive data presented as mean±SD; continuous data are analyzed by paired/unpaired 't' tests; and Chi-square test to assess the statistical difference between the two groups; Mann-Whitney U test; Chi square test; Wilcoxan test; and inter mixed analysis.

RESULTS

2 hours

The mean pain±standard deviation (NRS) at 2 hour is 0.56±1.459 in solution A and 0.10±0.303 in solution B. On applying Mann Whitney U-test, we have found that the p-value is less than 0.05 (0.045), so there is mean pain (NRS) at 2 hours in solution A and B has statistically significant difference.

4 hours

The mean pain±standard deviation (NRS) at 4 hour is 1.70±2.435 in solution A and 1.42±2.041 in solution B. On applying Mann Whitney U-test, we have found that the p value is greater than 0.05 (0.834), so there is mean pain (NRS) at 4 hour in solution A and B has no statistically significant difference.

6 hours

The mean pain±standard deviation (NRS) at 6 hour is 2.16±2.566 in solution A and 2.54±2.712 in solution B. On applying Mann Whitney U-test, we have found that the p-value is greater than 0.05 (0.428), so there is mean pain (NRS) at 6 hours in solution A and B has no statistically significant difference.

12 hours

The mean pain±standard deviation (NRS) at 12 hour is 1.04±1.829 in solution A and 0.62±0.923 in solution B. On applying Mann Whitney U-test, we have found that the p value is greater than 0.05 (0.911), so there is mean pain (NRS) at 12 hours in solution A and B has no statistically significant difference.

24 hours

The mean pain±standard deviation (NRS) at 24 hours is 1.44±2.604 in solution A and 0.22±0.582 in solution B. On applying Mann Whitney U-test, we have found that the p value is less than 0.05 (0.012), so there is mean pain (NRS) at 24 hours in solution A and B has statistically significant difference.

36 hours

The mean pain±standard deviation (NRS) at 36 hour is 1.56±2.635 in solution A and 0.14±0.452 in solution B. On applying Mann Whitney U-test, we have found that the p value is less than 0.05 (0.001), so there is mean pain (NRS) at 36 hours in solution A and B has statistically significant difference.

48 hours

The mean pain±standard deviation (NRS) at 48 hour is 0.48±1.266 in solution A and 0.18±0.596 in solution B. On

applying Mann Whitney U-test, we have found that the p value is greater than 0.05 (0.075), so there is mean pain (NRS) at 48 hours in solution A and B has no statistically significant difference.

72 hours

The mean pain±standard deviation (NRS) at 72 hour is 0.54±1.313 in solution A and 0.12±0.435 in solution B. On applying Mann Whitney U-test, we have found that the p value is greater than 0.05 (0.106), so there is mean pain (NRS) at 72 hours in solution A and B has no statistically significant difference.

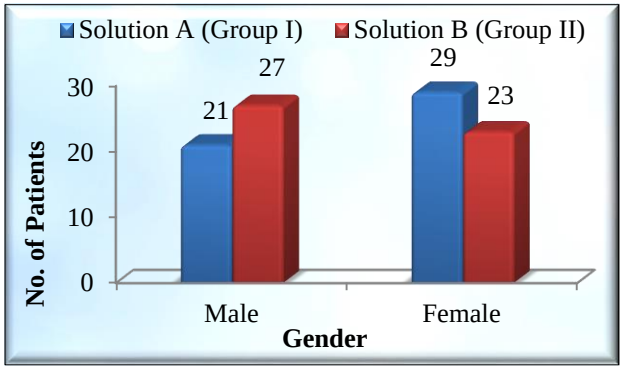

Figure 1: Number of males and females in different groups.

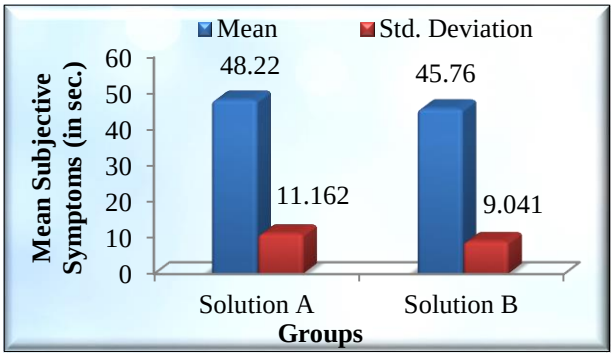

Figure 2: Onset of symptoms in seconds after administration of local anaesthesia.

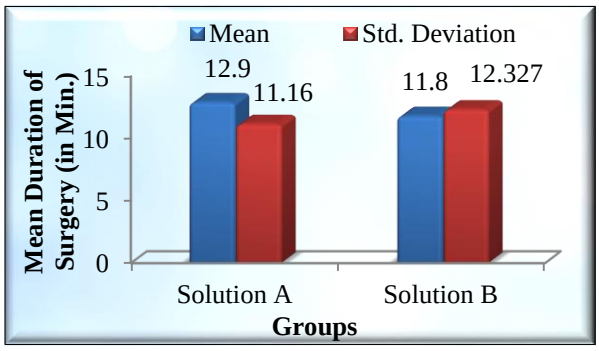

Figure 3: Duration of surgery.

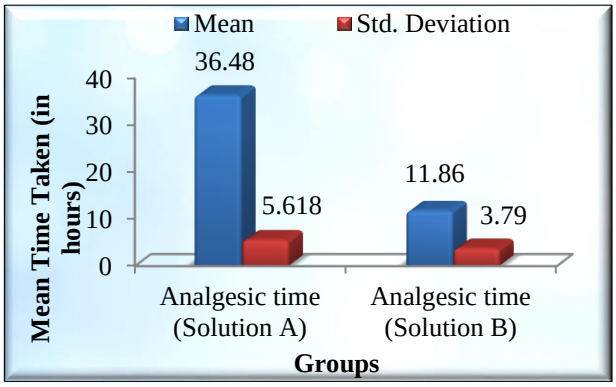

Figure 4: Duration of analgesia in hours for solution A and solution B.

Inference

The pain was found to be statistically significant at 2 hours, 24 hours and 36 hours postoperatively, thereafter the difference in NRS values between the solutions was not significant. Hence, the analgesic effect of solution A (buprenorphine) was effective at 2 hours, 24 hours and 36 hours postoperatively.

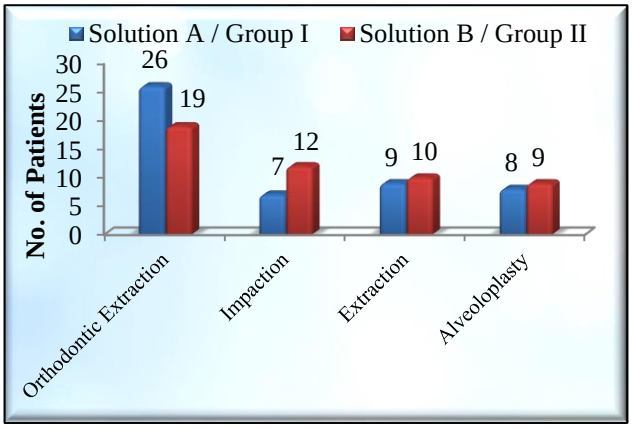

Figure 5: Different minor surgical performed in patients of solution A and solution B.

DISCUSSION

Pain is one of the most common vital symptoms in oral and maxillofacial surgery. It is a major concern to the surgeon as well as patients due to a considerable degree of inflammatory response involved in the surgical procedure. The management of post-operative pain remains an arena for never ending research, with better formulations and modalities continuously replacing the obsolete ones.

NSAIDs are the most commonly used analgesics agents after oral surgery, as most cases of post-operative dental pain include an inflammatory component. For this reason, NSAIDs are the most rational first-line analgesic and inflammatory agents all over the world. However, one of the most frequent side effects of NSAIDs is

gastrointestinal toxicity. Prostaglandins are required for stimulating the production of mucosal lining that protects the stomach and small intestine. NSAIDs act by inhibiting the synthesis of these particular prostaglandins, thereby leading to erosive and ulcerative side effects on the gastro-intestinal mucosa. This erosive and ulcerative action is enhanced by the fact that orally administered drug lies in contact with gastric mucosa.[9]

Various researches are being conducted in the field of pain medicine to discover newer drugs which could reduce the use of NSAIDs yet give an effective analgesia. Several studies have suggested that addition of certain opioids to the local anesthetic solution used for block anesthesia to provide effective and prolonged post-operative analgesia. The addition of opioids like buprenorphine to 2% lignocaine hydrochloride (LA) has been shown to reduce the use of NSAIDs post-operatively. It has been also shown that the presence of opioid receptors in peripheral nervous system offers the possibility of providing good post-operative analgesia in ambulatory surgical patients.[3,4,6-8]

Modi et al and Candido et al conducted a study on the efficacy of addition of buprenorphine to local anesthesia in providing prolonged postoperative analgesia. They showed that when added buprenorphine is added to 0.5% bupivacaine with epinephrine 1:200,000, the anesthetic efficacy increases. However, since bupivacaine is a long-acting anesthetic, the action of buprenorphine will be masked.[9,10]

Buprenorphine has been used as an opioid drug mixed with local anesthetic because buprenorphine is highly lipophilic; hence it better diffuses into the perineurium and produces longer effect of analgesia compared to morphine and sufentanil. buprenorphine hydrochloride is at least 30 or 50 times more potent than morphine sulphate, according to various studies published, and has a substantially longer duration of action.[10]

In 1969, researcher Reckitt Benckiser spent 10 years attempting to synthesize an opioid compound "with structures substantially more complex than morphine that could retain the desirable actions whilst shedding the undesirable side effects (addiction)." Reckitt found success when researchers synthesized RX6029 which had showed success in reducing dependence in test animals. RX6029 was named buprenorphine and began trials on humans in 1971. By 1978 buprenorphine was first launched in the UK as an injection to treat severe pain, with a sublingual formulation released in 1982.[8,13,14]

For the present study lignocaine 2% with adrenaline 1:200000 was taken as an anesthetic solution since it was easily available and used in most dental setups. 2% lignocaine with adrenaline 1:200000 produced anesthesia for 1 hour which is of sufficient duration to complete most of the routine minor oral surgical procedures. In our study there was no significant difference in onset of subjective symptoms between the two groups of solution A and solution B, with mean value of 48.22 seconds and 45.76 seconds respectively. A similar trend was noted in onset of objective signs between the two groups, with mean value of 59.22 seconds and 53.36 seconds respectively. This is in accordance with a study done by Kumar et al on the efficacy of buprenorphine added lignocaine 2% in providing postoperative analgesia after minor oral surgery. Similar results have been reported by Modi et al. Candido et al have seen the efficacy of buprenorphine in providing prolonged postoperative analgesia when added to a mixture of 1% mepivacaine and 0.2% tetracaine with epinephrine 1:200,000, and have found similar results.[7,9,10,15]

In our study post-operative analgesia in solution A (buprenorphine mixed with lignocaine) is more than solution B (lignocaine). The mean value of post-operative analgesia in solution A was (36.48 hours) and solution B was (11.86 hours) respectively. Further it was supported by number of rescue medication taken by patients in solution A and solution B and their mean was (2.78 tablets) and (3.66 tablets). Similar results have been showed by Bazin et al, who studied the effect of addition of morphine, buprenorphine and sulfetanil to local anesthetic in brachial plexus block. The results obtained showed that addition of morphine or buprenorphine to local anesthetic produced significant difference in duration of analgesia when compared to the control group, wherein only local anesthetic was used. The number of rescue medications taken was less for buprenorphine (21 tablets) than morphine (38 tablets) and sufentanil (29 tablets). Similar results were found in a study done by Kumar et al, where group I (buprenorphine mixed with lignocaine) patients had significantly.[7,16]

Modi et al researched that buprenorphine added to the local anesthetic injected in performing various intraoral nerve blocks does provide prolonged postoperative analgesia and markedly decreases the need for pain medication in the early and late postoperative periods, at least up to 48 hours. Furthermore, the addition of Buprenorphine to the local anesthetic mixture used in this study did provide 3 times the duration of analgesia provided by the local anesthetics alone. The mean duration of postoperative analgesia in group II (28.18±1.02 hours) was 3 times greater than that in group I (8.34±0.11 hours). This difference was found to be a statistically highly significant difference, ($p<0.001$). Viel et al compared the effect of buprenorphine with that of morphine added to 0.5% bupivacaine on the duration of analgesia after supraclavicular brachial plexus block. They found that the duration of analgesia produced by the addition of buprenorphine to bupivacaine was twice that produced by the addition of morphine, In the study done by Candido et al the mean duration of postoperative analgesia in group II (buprenorphine mixed with bupivacaine) (17.4±1.26 hours) was 3 times greater than that in group I (bupivacaine alone) (5.3±0.15 hours), a highly significant difference, both statistically ($p<0.001$) and clinically, which was again in accordance to our study.[9,10,17]

In our study 5 patients had vomiting and nausea as a post-operative complication in buprenorphine group or solution A, which was contradictory to study done by Kumar et al who noted that none of the patients in either group reported opioid-related side effects such as nausea, vomiting, or pruritus or showed any evidence of respiratory depression. The absence of side effects may be attributed to the fact that 1 ml of the solution contained as little as 0.01 mg of buprenorphine. Modi et al found that none of the patients in either group reported opioid-related side effects such as nausea, vomiting, or pruritus or showed any evidence of respiratory depression.[7,10]

Limitations

Further studies and clinical trials are required for appraisal of these drugs with larger sample size.

CONCLUSION

Observations were made to assess and compare the onset of subjective and objective symptoms of anesthesia, duration of anesthesia and onset of pain for the solution A and B. Patients were also assessed on NRS for post-operative pain. Statistical analysis was done.

The results obtained showed that there was no statistically significant difference in the onset of anesthesia and also on duration of anesthesia in patients who receiving either local anesthetic agent with or without buprenorphine. However, there was statistically significant difference in duration of analgesia or the time at which first rescue medication was taken. The duration of analgesia for the patients who received buprenorphine was approximately three times more than that of only local anesthetics. The total number of analgesic tablets taken by the patients was significantly less with buprenorphine.

The results of our study concluded that addition of 0.3 mg of buprenorphine to local anesthetic solution provides efficient post-operative analgesia and reduces patient's discomfort. The requirement of number of post-operative NSAIDs tablet also decreased considerably and hence, the gastro intestinal side effects of NSAIDs. Buprenorphine, however, induced side effects such as nausea, vomiting, headache and dizziness in 5 patients out of 50.

Much research is required to be done on the use of buprenorphine with local anesthetic solution for post-operative pain management in dentistry.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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