

Comparative analysis of post operative analgesic requirement in patient undergoing minor oral surgery using buprenorphine with lignocaine versus lignocaine - a double blind study

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ABSTRACT

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Received: 18/02/2015

Accepted: 10/07/2015

Aim: The aim of this study is comparative analysis of post operative analgesic requirement in patient undergoing minor oral surgery using 2% Lignocaine with 1:200000 Adrenaline and Buprenorphine versus 2% lignocaine with 1:200000 Adrenaline.

Materials and Method: One hundred 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allocations. 1 ml of Buprenorphine Hydrochloride injection I.V which contains an equivalent of 0.3 mg Buprenorphine was withdrawn into a syringe and injected into a 30 ml vial of 2 % Lignocaine with Adrenaline 1:200000. Thus each ml of local anesthetic contained 0.01 mg of Buprenorphine. This solution was labelled and used for the study.

Results: The duration of analgesia in Group I was found to be 13.71 ± 7.2 h and Group II was $39.58 \pm$ the average consumption of NSAIDs was found to be 2.88 as compared to Group II mean value of 1.29 ($P=0.0001$).

Conclusion: We concluded that addition of 0.3 mg of Buprenorphine to 30 ml Lignocaine with Adrenaline 1:200000 for minor oral surgery results in significant improvement in postoperative analgesia up to 39 h and markedly reduces the need for excessive analgesic intake. Thus reducing the adverse effects associated with excessive use of NSAIDs. Further studies needs to be done as there is less literature about Buprenorphine added to local anaesthetist.

Keyword: Buprenorphine, Hydrochloride, Analgesia

INTRODUCTION

Pain is an unpleasant emotional experience usually initiated by a noxious stimulus and transmitted over a specialised neural network to the central nervous system where it is interpreted as such.¹ 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. Buprenorphine, first synthesized in 1966, is a semisynthetic, oripavine alkaloid derived from thebaine and binds to all three receptors.²

Buprenorphine is highly lipophilic and is better diffused into the perineurium.^{2,3} It produces longer effect of analgesia compared to Morphine and sufentanil. It is at least 30 times more potent than Morphine Sulphate and has substantially longer duration of action. This prolonged duration appears to be because Buprenorphine seems to dissociate very slowly from opioid receptors, so the usual duration of action is about eight hours after parenteral administration.^{4,5} Few studies have been conducted in past which prove the efficacy of Buprenorphine in Bupivacaine as a post operative analgesic in minor oral surgery.³ Bupivacaine has longer duration of action itself so it is difficult to analyse whether post operative analgesic effect in minor oral surgical procedure is due to the effect of Bupivacaine or Buprenorphine. Kumar SP 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, alveoloplasty, third molar surgery, incision and drainage of abscess There is paucity of literature regarding the use of combination of Buprenorphine

Access this article online	
Quick Response Code:	Website: www.its-jds.in
	DOI: 10.5958/2393-9834.2015.00008.X

and 2% Lignocaine with 1:200000 Adrenaline in minor oral surgical procedures. In our study we compared onset, quality and duration of post operative analgesia of Buprenorphine along with 2% Lignocaine with 1:200000 Adrenaline versus 2% Lignocaine with 1:200000 Adrenaline in minor oral surgical procedures.^{6,7,8,9}

MATERIALS AND METHOD

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. One hundred 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.

Method of Preparation of the Solution

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. Thus each ml of local anesthetic contained 0.01 mg of Buprenorphine. This solution was labelled and used for the study.

Study Design

Double blinding of the operator and patient was achieved by appointing a custodian who was not 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, a copy of which is attached as Annexure 1.

One of the solutions had 2 % Lignocaine Hydrochloride with 1:200000 Adrenaline Bitartrate along with Buprinorphine 0.3mg and other had 2 % Lignocaine Hydrochloride with 1:200000 Adrenaline Bitartrate for intra oral nerve block to achieve local anesthesia.

Table – 1: Different minor surgical performed in patients of two groups

	Solution A/ Group I	Solution B/ Group II
ORTHODONTIC EXTRACTION	32	30
IMPACTION EXTRACTION	6	16
ALVEOLOPLASTY	4	4

Table – 2: Number of different nerve blocks given in two groups

	Solution A/ Group I	Solution B/ Group II
INFRA ORBITAL	15	15
INFERIOR ALVEOLAR	18	17
NASO PALATINE	3	1
GREATER PALATINE	18	19
POSTERIOR SUPERIOR ALVEOLAR	6	6
LONG BUCCAL	3	8

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 postoperative analgesics consumed during the next 72 hours, at intervals of 2, 4, 6, 12, 24, 36 and 48h, 72h. Patients daily rating of discomfort was done on a 3-point, Numeric Rating Scale; (NPRS scale).

Patients were instructed to document the number of rescue medication consumed and the timing of first analgesic intake during the study period.

3ml of solution was used for every nerve block given in this study.

Data Analysis

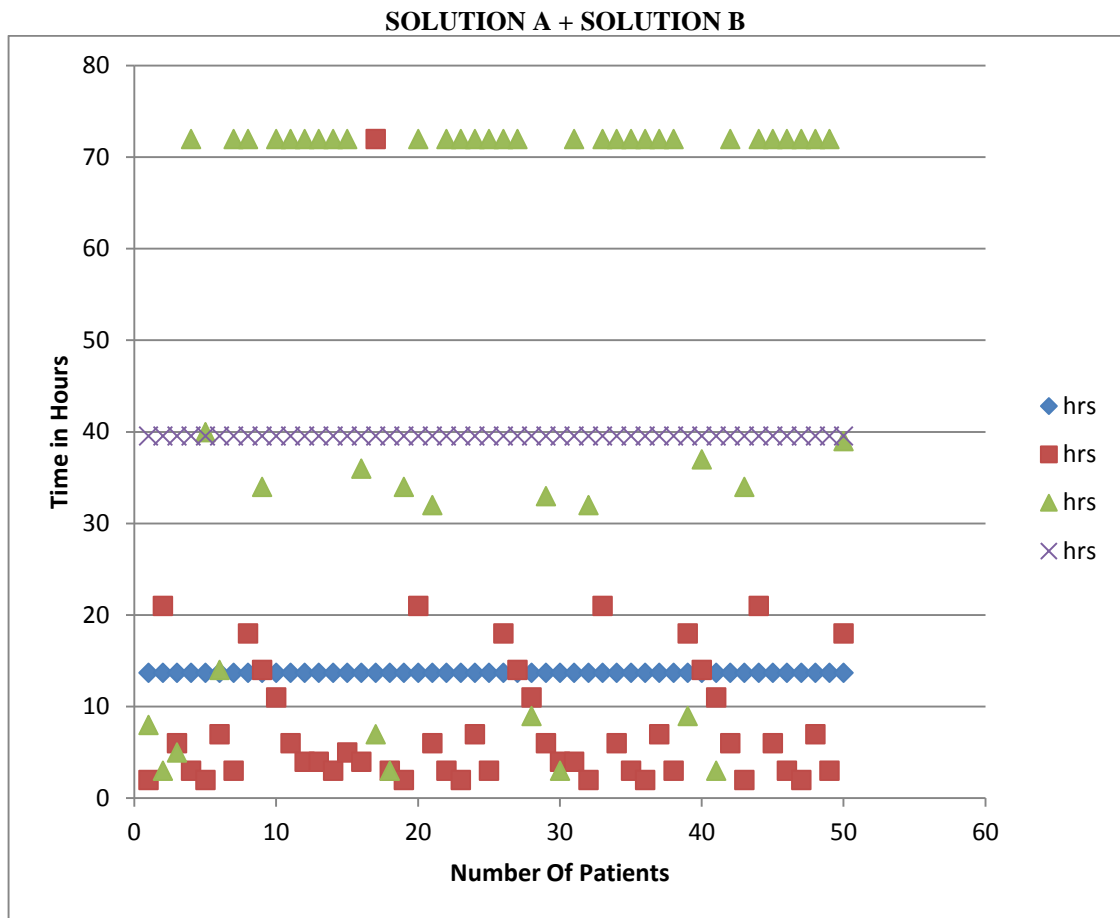
Results were calculated using the mean value and standard deviation for each of the parameters considered and checked for statistical significance using the following:-

1. Descriptive data presented as mean ± SD
2. Continuous data are analyzed by paired / unpaired ‘t’ tests
3. Chi-square test to assess the statistical difference between the two groups.
4. Mann–Whitney U test.
5. Chi square test
6. Wilcoxon test
7. Inter mixed analysis

RESULTS

The mean onset of subjective symptoms for Solution A was 42.54 seconds and the mean onset of subjective symptoms for Solution B was 47.79 seconds. On applying t-test the mean difference (5.250) was not significant (p = 0.697) indicating that the mean time of onset for subjective symptoms in solution A and solution B are comparable.

The mean duration of anaesthesia for Solution A was 224.13 minutes, and the mean of duration of anaesthesia for Solution B was 230.17 min. On applying t-test the mean difference (6.041) is not significant as p = 0.727 (p > 0.05) therefore duration of anaesthesia in minutes of solution A and of solution B have no significant difference.

Table - 3: Time at Which First Rescue Medication Taken (Duration of Analgesia)**GRAPH- 5 Showing Duration of Analgesia in Minutes in Solution A and Solution B**

- ▲ Each Patient Reading in Solution A
- Each Patient Reading in Solution B
- × Mean Reading in Solution B
- ◆ Mean Reading in Solution A

The mean of total number on analgesic tablets taken for Solution A was 2.88 tablets and the mean of total number on analgesic tablets taken for Solution B in minutes was 1.29 tablets. On applying t-test the mean difference (1.596) is significant as $p = 0.022$ ($p < 0.05$) indicating that there was a significant difference in the requirement of postoperative pain control for solution A as compared to solution B. The patient who received solution A took more tablets for pain control as compared to those who receive solution B gives more post operative analgesia.

Three patients (6%) in Solution B out of 50 reported of nausea, severe vomiting and dizziness and 3% out of 100 patients reported of side effects.

DISCUSSION

In recent years, there has been an increase awareness of the importance of effective pain management.

Although the currently available armamentarium of analgesic drugs and techniques is impressive, postoperative pain is not always effectively treated.^{10,11,12,13} Routinely the patients undergoing minor oral surgical procedures are prescribed some form of NSAIDs to overcome the sequel of postoperative pain.^{14,15,16}

Pain may be described as an unpleasant sensory and emotional experience associated with actual or potential tissue damage.^{3,4,17} Pain itself is subject to much inter individual variability with regard to threshold and tolerance and has exceptional and emotional components.^{18,19,20}

Hence arises, the need for an agent which reduces postoperative pain and additional intake of NSAIDs which in turn shall help in negating the adverse effects resulting due to excessive use of NSAIDs.^{21,22}

Over the past ten years several studies have suggested that addition of certain opiates to the local anesthetic used for block anesthesia may provide effective and prolonged post-operative analgesia.²³ The presence of opioid receptors in peripheral nervous system offers the possibility of providing postoperative analgesia in ambulatory surgical patients.^{24,25}

One of major problems in developing countries in the speciality of anaesthesia is the availability of drugs. Buprenorphine is not easily available in country, pethidine¹³ and Morphine are other drugs, the availability of which can be problem as both these drugs are subjected to Controlled Drugs Act with only a certain quota released to hospital at variable interval.^{26,27} Its low abuse potential, its cardiovascular stability, longer duration of action, and its potential safety in over dosage outweigh its disadvantages especially in major surgery and in situations where shorter acting drugs are not available.^{26,28,29}

Buprenorphine is an FDA approved drug that is used to treat opiate dependence and prevent its relapse. It was first synthesized in 1966. Buprenorphine is a semisynthetic, oripavine alkaloid derived from Thebaine. It is long acting, lipid soluble, mixed agonist antagonist opioid analgesic, which is at least 25 to 50 times more potent than Morphine. Buprenorphine was one of the first narcotic analgesics to be studied for its abuse liability in humans²². Thus, an intramuscular injection of Buprenorphine 0.3 mg is equipotent to morphine 10 mg, but the analgesia produced by Buprenorphine lasts significantly longer. A ceiling effect for respiratory depression but not for analgesia has been demonstrated in humans.^{30,31}

This prolonged duration appears to be because buprenorphine seems to dissociate very slowly from opioid receptors, so the usual duration of action is about 8 hours after parenteral administration.³² Buprenorphine was initially classified as mixed agonist-antagonist analgesia or as a narcotic antagonist analgesic in most preclinical anti-nociceptive tests; Buprenorphine was shown to be fully efficacious, with an antinociceptive potency 20 to 70 times higher than that of Morphine.^{23,27}

Viel et al in 1998 the investigators compared the effect of Buprenorphine with that of morphine added to 0.5% Bupivacaine on the duration of analgesia after supraclavicular brachial plexus block.¹¹ A study by Romero et al indicated that the mean terminal half-life of intravenously given Buprenorphine (1 mg infused over 30 minutes) was about 6 hours.³³ Kuhlman et al reported a mean terminal half-life of 3.2 hours after single doses of 1.2 mg given intravenously.

Sittl et al in 2006 suggested that Buprenorphine has an antinociceptive potency about 75 to 100 times greater than that of morphine. Buprenorphine has a dose-dependent effect on analgesia with no

respiratory depression. Dahan and colleagues in 2006 demonstrated that Buprenorphine has a ceiling effect on respiratory depression, but not on analgesia. This was demonstrated over a dose range of 0.05 to 0.6 mg Buprenorphine in humans. Buprenorphine shows analgesic effects, but no respiratory depression, at doses up to 10 mg. Therefore, Buprenorphine may have a differential effect on respiration and analgesia.³⁴ Bazin et al. 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. Similar results were found in our study, where Group I patients had significantly lesser mean pain scores at varying time intervals postoperatively (up to 33 ± 1.5 h) compared to Group II patients. Mean pain scores obtained at 48 and 72 h postoperatively did not vary significantly in Group I compared to the Group.^{11,12}

In the present study, a clinical prospective randomised double blind study was conducted of 100 patients undergoing minor oral surgical procedures. Each patient was anesthetized by using either Solution A or B after taking informed consent and the parameters decided as per the performance recorded. Double blinding of the operator and patient was achieved by appointing a custodian who was not 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 solutions had 2 % Lignocaine Hydrochloride with 1:200000 Adrenaline Bitartrate along with Buprenorphine 0.3mg and other had 2 % Lignocaine Hydrochloride with 1:200000 Adrenaline Bitartrate for intra oral nerve block to achieve local anesthesia²².

The mean \pm standard deviation of onset of anesthesia time in seconds of subjective symptoms are (42 ± 12.364 seconds) and (47.79 ± 14.479 seconds) in Solution A and Solution B respectively.

On applying t-test the mean difference (5.250) is not significant as $p = 0.697$ ($p > 0.05$) indicating that the mean time of onset of anaesthesia in solution A and solution B are comparable.

The mean \pm standard deviation of onset of anesthesia time in seconds of objective signs are (49.88 ± 9.786 seconds) and (53.83 ± 15.262 seconds) in Solution A and Solution B respectively.

On applying t-test the mean difference (3.95) is not significant as $p = 0.709$ ($p > 0.05$) indicating that the mean time of onset of anaesthesia in solution A and solution B are also comparable.

The mean \pm standard duration of surgery in minutes are (8.17 \pm 8.579 minutes) and (9.42 \pm 8.382 minutes) performed under the effect of Solution A and Solution B respectively.

On applying t-test the mean difference (1.25) is not significant as $p = 0.813$ ($p > 0.05$) indicating that duration of surgery performed under the effect of both solutions, A and B was similar and statistically not significant.

The mean \pm standard duration of anesthesia in minutes are (224.13 \pm 22.142 minutes) and (230.17 \pm 30.792 minutes) in Solution A and Solution B respectively.

On applying t-test the mean difference (6.041) is not significant as $p = 0.727$ ($p > 0.05$) so we can say that duration of surgery in minutes of solution A and solution B have no significant difference.

The mean \pm standard of total number of analgesic medication taken per day until follow up after 72 hours were (2.88 \pm 1.424 tablets) and (1.29 \pm 1.922 tablets) for Solution A and Solution B respectively.

On applying t-test the mean difference (1.596) is significant as $p = 0.022$ ($p < 0.05$) indicating that there was a significant difference in the requirement of postoperative pain control for Solution A and Solution B.

Three patients (6%) in Solution B out of 50 reported of nausea, severe vomiting and dizziness and 3% out of 100 patients reported of side effects.

The mean \pm standard of post surgical analgesia was (13.71 \pm 7.95 hours) and (39.58 \pm 1.922 hours) for Solution A and Solution B respectively. On applying t-test the mean difference (2.587) was significant as $p = 0.028$ ($p < 0.05$) indicating duration of analgesia differed significantly for Solution A and Solution B.

We concluded that addition of 0.3 mg of Buprenorphine to 30 ml Lignocaine with Adrenaline 1:200000 for minor oral surgery results in significant improvement in postoperative analgesia up to 39 h and markedly reduces the need for excessive analgesic intake. Thus reducing the adverse effects associated with excessive use of NSAIDs. Further studies needs to be done as there is less literature about Buprenorphine added to local anaesthetist.

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How to cite this article: Thukral H, Singh S, Aggarwal A, Kumar S, Mishra V, Anand KR. Comparative analysis of post operative analgesic requirement in patient undergoing minor oral surgery using buprenorphine with lignocaine versus lignocaine - a double blind study. J Dent Specialities, 2015;3(2):164-169.

Source of Support: NIL

Conflict of Interest: All authors report no conflict of interest related to this study.