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CLINICAL STUDY

Efficacy of Buprenorphine Added 2 % Lignocaine 1:80000 in Postoperative Analgesia After Minor Oral Surgery

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Abstract
Purpose Recent studies have demonstrated that opioid analgesia cannot be exclusively attributed to effects within central nervous system. Peripheral opioid receptors exist that can be activated by locally applied opioid agonists which mediate analgesic effects that are particularly prominent in painful inflammatory conditions. Patients who present themselves with conditions requiring minor surgery in the maxillo-facial region usually have associated ongoing inflammatory process. The aim of our study was to apply the concept of peripheral opioid analgesia in minor oral surgery and evaluate its effectiveness in managing postoperative pain. The present study was designed to evaluate the efficacy of buprenorphine added lignocaine 2 % in providing postoperative analgesia after minor oral surgery.
Materials and Methods Hundred consenting adult patients who were scheduled to undergo various minor oral surgeries were enrolled in this double blinded study. Patients were randomly assigned into one of the two groups based on whether they received buprenorphine added 2 % lignocaine 1:80000 (Group I) or (Group II) lignocaine 2 % with adrenaline 1:80000 alone. Visual analog scale method was used for evaluation of the postoperative analgesia.
Results The duration of analgesia in Group I was found to be 36 ± 1.5 h and the average consumption of NSAIDs was found to be 1.86 as compared to Group II mean value of 4.4 ($P < 0.0001$).
Conclusion Addition of small amounts of buprenorphine to 30 ml lignocaine with adrenaline 1:80000 for minor oral surgery results in significant improvement in postoperative analgesia up to 36 h and markedly reduces the need for excessive analgesic intake. Thus reducing the adverse effects associated with excessive use of NSAIDs.

Keywords Local anesthesia · Buprenorphine added LA · Peripheral opioid analgesia

Introduction

Over the past, several studies have suggested that addition of certain opiates to the local anesthetic solution used for block anesthesia may provide effective and prolonged postoperative analgesia [1–3]. The presence of opioid receptors in peripheral nervous system offers the possibility of providing postoperative analgesia 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 [4–6] and also in brachial plexus blocks [7–10]. Most of the studies pertaining to use of opioids mixed with local anesthetics were performed using 0.5 % bupivacaine which has longer duration of action. Most importantly the longer acting local anesthetic such as 0.5 % bupivacaine may overlap or obscure the analgesia provided by the opioids. This study was designed to utilize

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intermediately acting anesthetic such as lignocaine to determine the duration of postoperative analgesia after minor oral surgery.

The present study was under taken to determine efficacy of buprenorphine added 2 % lignocaine 1:80000 in providing post-operative analgesia in patients undergoing minor oral surgery and concomitantly evaluate its role in reducing the need for administration of non-steroidal anti-inflammatory drugs (NSAIDs).

Materials and Methods

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. 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 investigators to remain unaware of the group allocations. Criteria for exclusion included history of asthma, neurological or psychiatric disease, substance abuse or allergy to any of the medications used in the study. Patients entering the study were prohibited from taking any other analgesics other than the one used in the study. Patients who had consumed analgesics six hours prior to the surgical procedure were excluded from the study.

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 1:80000. Thus each ml of local anesthetic contained 0.01 mg of buprenorphine. This solution was labeled and was used for the study.

Study Design

The patients selected for the study were divided randomly into 2 groups, based solely on whether buprenorphine was to be added to the local anesthetic agent or not. Patients in Group I underwent the oral surgical procedure after administration of lignocaine 2 % with adrenaline 1:80000 to which 0.3 mg (1 ml) buprenorphine was added. Patients in Group II underwent the oral surgical procedure after administration of lignocaine 2 % with adrenaline 1:80000 alone. Various minor surgical procedures included in the study were third molar surgeries, alveoloplasties and cyst enucleations (refer Table 1). All surgical procedures were performed after administration of one of the two solutions used in the study. Standard intraoral nerve block techniques were utilized to achieve intra operative anesthesia. Post operatively all patients were prescribed tablet Diclofenac 50 mg as a rescue analgesic.

Table 1 Types of minor oral surgical procedures

Type of procedure	Number of patients	
	Group I	Group II
Third molar surgery	40	40
Alveoloplasty	5	5
Incision and drainage of abscess	3	3
Cyst enucleations	2	2

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 h, at intervals of 2, 4, 6, 12, 24, 36 and 48 and 72 h. Patients daily rating of discomfort was done on a 4-point, visual analogue scale; (VAS scale), interpreted as:

0 No pain
1 Mild pain
2 Moderate pain
3 Severe pain

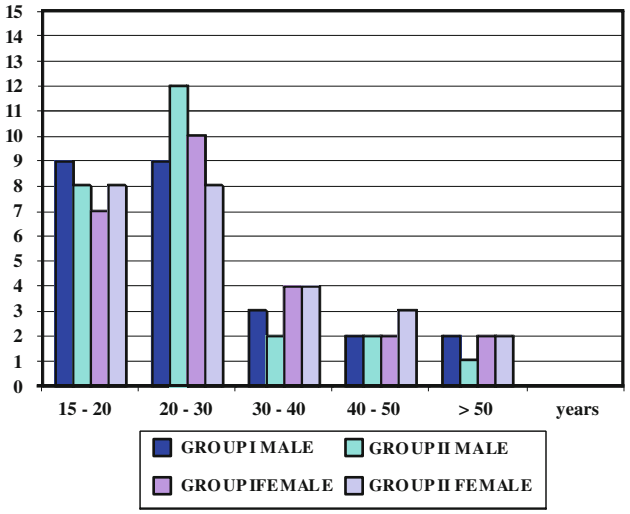
Patients were instructed to document the number of rescue analgesics consumed and the timing of first analgesic intake during the study period.

Data Analysis

The data obtained were evaluated based on the pain levels as marked by the patients in study group and control group using the Visual Analog Scale at intervals of 2, 4, 6, 12, 24, 36, 48 and 72 h interval. Total number of Diclofenac tablets taken in the 72 h period was also documented. Patients were considered to have completed the study at the time of first analgesic intake. Results were calculated using the mean value and standard deviation for each of the parameters considered and checked for statistical significance using the Mann–Whitney test.

Results

There were no significant differences between the two groups with respect to age and sex (refer Graph 1). Differences in VAS scores were analyzed using the Mann–Whitney test between both the groups, at each of the fixed time intervals. The mean pain level at 2 h in Group I



Graph 1 Showing age and sex distribution

compared to Group II was found to be significantly lower, *P* value <0.0001. Similar comparison of pain values at 4, 6, 12, 24 and at 36 h was found to be significantly lower in Group I (refer Table 2). The comparison of pain level values at 48 and 72 h time intervals did not vary statistically as shown (refer Table 3). The total number of analgesics consumed by patients in Group I was found to be significantly less compared to Group II patients. The patients in Group I had a consumed an average of 1.86 tablets as compared to Group II patients, average of 4.4 tablets in 72 h time period (*P* value <0.00001).

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. Routinely the patients undergoing minor oral surgical procedures are prescribed some form of NSAIDs to overcome the sequel of postoperative pain.

Although these drugs have been proven efficient in management of post-operative pain, adverse effects and associated morbidity pose a serious problem. It is therefore the duty of the clinician to reduce such problems associated with increased number of analgesic intake in the postoperative period. It has long been known that NSAIDs may have a range of side effects, of which the commonest are gastrointestinal. 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.

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 [7–10]. The presence of opioid receptors in peripheral nervous system offers the possibility of providing postoperative analgesia 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 anesthetic injected in inflamed dental tissues [4–6] and brachial plexus blocks [7–10]. The results of these studies showed that buprenorphine was effective perineurally and longer in duration of action in the management of post-operative pain in ambulatory surgical patients.

We have chosen lignocaine 2 % with adrenaline 1:80000 as an anesthetic solution since it is easily available and used in most dental setups. 2 % lignocaine with adrenaline 1:80000 produces anesthesia for 1½ h which is of sufficient duration to complete routine minor oral surgical procedures.

We have used buprenorphine as the opioid drug mixed with local anesthetic for the following reasons:

Table 2 Statistics of visual analog scale values obtained and its inferences

Time interval	Group 1		Group 2		*P* value
	Study group		Control group		
	Mean deviation	Standard deviation	Mean deviation	Standard deviation	
2 h	0.48	0.65	1.3	0.81	<0.0001
4 h	0.54	0.73	1.3	0.81	<0.0001
6 h	0.52	0.65	1	0.73	0.0022
12 h	0.64	0.85	1.26	0.92	0.0011
24 h	0.36	0.63	1.04	1.03	0.0007
36 h	0.36	0.69	0.76	0.62	0.0014
48 h	0.24	0.52	0.46	0.65	0.1192
72 h	0.2	0.4518	0.46	0.6455	0.1152
Total no. of pain killers	1.86	1.6037	4.4	1.7957	<0.0001

Table 3 Showing pain relief at various time intervals

Pain level	No. of patients at 2 h	No. of patients at 4 h	No. of patients at 6 h	No. of patients at 12 h	No. of patients at 24 h	No. of patients at 36 h	No. of patients at 48 h	No. of patients at 72 h
Group I								
No pain—0	30 (60 %)	30 (60 %)	28 (56 %)	29 (58 %)	36 (72 %)	37 (74 %)	40 (80 %)	41 (82 %)
Mild pain—1	16 (32 %)	13 (26 %)	18 (36 %)	11 (22 %)	10 (20 %)	9 (18 %)	8 (16 %)	6 (12 %)
Moderate pain—2	4 (8 %)	7 (14 %)	4 (8 %)	9 (18 %)	4 (8 %)	3 (6 %)	2 (4 %)	3 (6 %)
Severe pain—3	– (0 %)	– (0 %)	– (0 %)	1 (2 %)	– (0 %)	1 (2 %)	– (0 %)	– (0 %)
Group II								
No pain—0	11 (22 %)	11 (22 %)	13 (26 %)	10 (20 %)	18 (36 %)	17 (34 %)	31 (65 %)	31 (65 %)
Mild pain—1	13 (26 %)	13 (26 %)	24 (48 %)	23 (46 %)	19 (38 %)	28 (56 %)	15 (30 %)	15 (30 %)
Moderate pain—2	26 (52 %)	26 (52 %)	13 (26 %)	11 (22 %)	7 (14 %)	5 (10 %)	4 (8%)	4 (8%)
Severe pain—3	– (0 %)	– (0 %)	– (0 %)	6 (12 %)	7 (14 %)	– (0 %)	– (0 %)	– (0 %)

- 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 50 times more potent than morphine sulphate and has substantially longer duration of action [11–13].

Bazin et al. [3] 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 36 ± 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 II (refer Table 3).

Candido et al. [8] have studied the effect of buprenorphine added local anesthetic for brachial plexus block in patients undergoing upper extremity surgeries. The results obtained in their studies showed that the patients who received buprenorphine added local anesthetic had mean duration of postoperative analgesia which was 3 times greater than the group of patients who received local anesthetic alone. The results obtained by the authors suggested that 75 % of the patients who received buprenorphine added local anesthetic were completely pain free at the end of 30 h post-operatively and also the number of analgesics consumed by patients in whom the modified local anesthetic was used were significantly lower compared to the control group [8].

Similarly in our study 74 % of the patients in Group I were completely pain free at the end of 36 h time interval postoperatively compared to only 34 % in Group II. The total number of analgesic intake in Group I (mean value of 1.86) compared to Group II patients (mean value of 4.4) is significantly less which is similar to the author's results [8]. None of the patients in the study reported any opioid related side effects such as nausea, vomiting, and pruritus or showed any evidence of respiratory depression.

Candido et al. [9] carried out a study to specifically delineate the role of buprenorphine in peripherally mediated opioid analgesia as the previous study conducted by them did not control for potentially confounding factors such as the possibility that buprenorphine was affecting analgesia through intramuscular absorption or via spinal mechanism. The results of the above study showed that buprenorphine produced 3 times longer analgesia than local anesthetic block alone and twice as long as buprenorphine given by intramuscular injection plus local anesthetic block alone [9]. Our study did not evaluate the intramuscular effect, since it was already proven in many investigations carried out previously [9, 14–16].

In our study there were no significant changes related to the time of onset of anaesthesia. And also no adverse effects related to use of buprenorphine. 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.

The limitation of the present study was that the postoperative analgesia obtained in patients in Group I cannot be clearly attributed to perineural action of buprenorphine, as most of the nerve block techniques were combined with local infiltration of the area to block the peripheral nerve endings.

Conclusion

With the limitations of the above study it can be concluded that addition of 0.3 mg of buprenorphine to 30 ml of 2 %

lignocaine with adrenaline 1:80000 for use in minor oral surgery produces significant pain relief up to 36 h post-operatively. We conclude stating that buprenorphine added local anesthetic has definite benefits for relief of postoperative pain and in reducing analgesic intake after minor oral surgery.

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