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Efficacy of Buprenorphine for Postextraction Pain in Lower Third Molar Surgery: A Comparaive Study

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KEYWORDS

Buprenorphine, Postextraction, Molar Surgery

ABSTRACT:

Pain is one of the more nuanced aspects of human physiology and psychology. Studies done for them have emphasised the necessity of efficient pain management, the necessity of post-operative pain control, and the necessity of healthcare providers providing enough perioperative analgesia. 1 Postoperative pain may have a number of negative acute and long-term effects. The appropriate attenuation of perioperative pathophysiology during surgery by methods that minimise nociceptive inputs to the central nervous system is essential for the patient's health and surgical success. Numerous studies have shown that enhancing perioperative analgesia lowers risks and expedites healing following surgery. 2

INTRODUCTION

Pain is one of the more nuanced aspects of human physiology and psychology. Studies done for them have emphasised the necessity of efficient pain management, the necessity of post-operative pain control, and the necessity of healthcare providers providing enough perioperative analgesia. 1 Postoperative pain may have a number of negative acute and long-term effects. The appropriate attenuation of perioperative pathophysiology during surgery by methods that minimise nociceptive inputs to the central nervous system is essential for the patient's health and surgical success. Numerous studies have shown that enhancing perioperative analgesia lowers risks and expedites healing following surgery. 2

Thus, quality of life would be a priority in typical clinical studies to determine whether new medications and treatments might accomplish improvement in many aspects of the patient's life. Therefore, a more strong opioid with fewer adverse effects is chosen.3

Regional anaesthetic techniques are frequently used for different surgical operations, either alone or in combination with general anaesthetic, because they have several advantages over general anaesthesia. Unfortunately, there are some limitations on these techniques due to the local anaesthetics' time of action. The discovery of opioid "local analgesia" presents an

Journal of Chemical Health Risks

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opportunity to create brand-new analgesics with potent analgesic effects but no central side effects. 4 One method to get past this restriction is to add adjuvant to the local anaesthetic solution. Many medications have been used as adjuvants, including clonidine, dexamethasone, magnesium, and buprenorphine, to lengthen the duration of action and eliminate post-operative analgesics, including buprenorphine. 5,4

It was granted US medical approval in 1981 after being patented in 1965. It is an extremely lipophilic derivative of oripavine's oripavine, the source of the opiate alkaloid thebaine (paramorphine). It is 25 to 40 times more potent as an anti-nociceptive medication than morphine after parenteral injection and 7 to 10 times more potent after oral treatment in rodents, where it has a rapid onset and prolonged duration of action. One of the most important characteristics of buprenorphine is that it has a ceiling effect for analgesia without causing direct organ damage at high doses.

Prospective double blind, randomized study was conducted on healthy volunteers (asa-i) irrespective of gender, race and caste reporting to the department of oral and maxillofacial surgery

sample size: 25 patients (50 surgical sites)

group 1 (study group): patients who received buprenorphine 0.01mg per ml of lignocaine 2% with adrenaline 1: 80,000 for inferior alveolar nerve block.

group 2 (control group): patients who received lignocaine 2% with adrenaline 1: 80,000 alone for inferior alveolar nerve block.

criteria for selection of the study subjects:

inclusion criteria: healthy individuals, aged above 18 years of either sex (asa class i and class ii), patients with bilaterally impacted mandibular third molars indicated for surgical removal, patient who were ready to sign the informed written consent to carry out the intervention and for inclusion in the study.

exclusion criteria: patient having clinically significant medical history and falling in category asa other than i and ii (eg. systemic infective disease, haematological disease, deficiency of coagulation, diabetes and neoplastic disease), who are allergic to amide type of local anaesthesia, known to be allergic to opioid analgesic or alcohol addiction, having a history of head injury, metabolic disorder, hypertension, epilepsy or other seizure disorder, and who were on antidepressant, muscle relaxant, narcotic, antipsychotic or medicine taking for nausea and vomiting, pregnant and lactating women.

materials:

- local anesthesia 2% lignocaine hydrochloride with adrenaline 1:80000
- 0.3 mg buprenorphine hydrochloride injection

methodology:

patients attending opd of department of oral and maxillofacial surgery indicated for impacted bilateral mandibular third molar surgery were considered for the study. detailed case history was recorded and evaluated for physical status. all potential participants were explained about the need and design of study, the buprenorphine, and its advantages and disadvantages. due informed written consent was taken prior. this was a double blind study neither the surgeon nor the patients were aware of the local anesthetic being tested. all surgeries and measurements were performed by the same surgeon and were healthy volunteers randomly divided into 2 groups according to the local anaesthetic solution used.

group 1 (study group): patients who received buprenorphine 0.01mg per ml of lignocaine 2% with adrenaline 1: 80,000 for inferior alveolar nerve block.

group 2 (control group): patients who received lignocaine 2% with adrenaline 1: 80,000 alone for inferior alveolar nerve block.

a pulse oximeter was used during the procedure to observe 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 had 0.01 mg of buprenorphine. for nerve block, preparation of the solution was done by qualified dental staff nurse

Journal of Chemical Health Risks

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for nerve block during the procedure. thus, the operator was remained unaware of the solution used in the patient.

the standard inferior alveolar, lingual and long buccal nerve block technique was employed to anesthetize surgical site of the impacted mandibular 3rd molar which was to be surgically removed.

on an average 3ml of local anaesthetic solution was injected in both groups, which meant a total of 0.03mg of buprenorphine was injected into each patient in study group for nerve block. all patients received anaesthetic solution at same rate. post operatively all patients were prescribed rescue analgesic tab. 50mg diclofenac sodium. after administration of local anaesthetic, following parameters were recorded in the proforma**:**

onset of anaesthesia:

numbness recorded as a subjective sensation of lip anaesthesia which was reported on questioning. presence of pain was determined by pin prick test using 0.8 mm sterile injection needle applied to attached gingiva, in standard manner. it is the time required from end of injection to the time point when pain to pinprick was abolished and numbness was positive.

duration and severity of postoperative analgesia:

the time of duration of anaesthesia was measured from the time subjective symptoms (numbness) were positive till the pain in the surgical area was felt. the pain was assessed every 2 h upto 24 h and then at 36, 48, and 72h.

severity of postoperative pain was evaluated when the patient first time felt pain by using explained vas scale by placing a mark on the line corresponding to their current level of pain.

number of rescue analgesics:

patients were instructed to document the number of rescue analgesics consumed during the study period

RESULT

a total of 25 patients (50 surgical sites) requiring surgical removal of impacted mandibular third molar under local anaesthesia were enrolled for this study and two different local anaesthetic solutions were used. the observations were noted during and after the administration of local anaesthetic solution. patients were divided in two groups.

group i (study group): patients who received buprenorphine 0.01mg per ml of lignocaine 2% with adrenaline 1: 80,000 for inferior alveolar nerve block.

group ii (control group): patients who received lignocaine 2% with adrenaline 1: 80,000 alone for inferior alveolar nerve block.

the age range 19 years – 58 years mainly in both groups. (table – i, graph- i). mean age of male patient was 28.60(sd:5.174) and 30.53(sd: 8.601) for female. both sexes were equally involved in the study 11 were males and 14 were females. (table – i, graph- i)

3.time of onset of anaesthesia:

the mean time of onset of anaesthesia (seconds) for group-i was 78.96 (sd: 11.61) versus 86.92 (sd: 18.51) for group-ii. statistically insignificant differences were observed between the two anaesthetic solutions. ($p < 0.075$) (table – ii, graph- ii).

4.duration of analgesia:

the mean duration of analgesia (hours) for group-i was 37.28(sd: 22.07) versus 4.48 (sd: 1.60) for group-ii. statistically significant differences were observed between the two anaesthetic solutions. ($p = 0.000$) (table – ii, graph- iii).

5.postoperative need of rescue analgesic consumption:

the mean need of postoperative analgesic for group-i was 5.72(sd: 3.42) versus 9.76 (sd:2.55) for group-ii. statistically significant differences were observed between the two anaesthetic solutions. ($p = 0.000$) (table – ii, graph- iv).

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(1), 594-601 | ISSN:2251-6727

6.severity of pain (checked by vas scale):

the mean severity of pain for group-i was 3.48(sd: 2.90) versus 7.56 (sd:1.36) for group-ii. statistically significant differences were observed between the two anaesthetic solutions. (p = 0.000) (table – ii, graph- v).

TABLES

TABLE I

sex		n	mean	std. deviation
age	male	10	28.60	5.147
	female	15	30.53	8.601

TABLE II:

site		N	Mean	Std. deviation	Std. Error Mean	Mean Difference	P value
onset of action(seconds)	control	25	86.92	18.51	3.701	7.96	0.075
	study	25	78.96	11.61	2.322		
duration of analgesia(hours)	control	25	4.48	1.60	0.321	-32.80	0.000 Statistical significant
	study	25	37.28	22.07	4.413		
number of rescue medications taken by patient (within 72 hrs)	control	25	9.76	2.55	0.511	4.04	0.000 Statistical significant
	study	25	5.72	3.42	0.684		
Severity of postoperative pain	control	25	7.56	1.36	0.271	4.08	0.000 Stastiscal significant
	study	25	3.48	2.90	0.581		

Independent samples T-test

Journal of Chemical Health Risks

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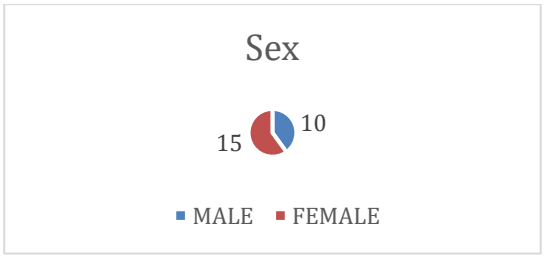
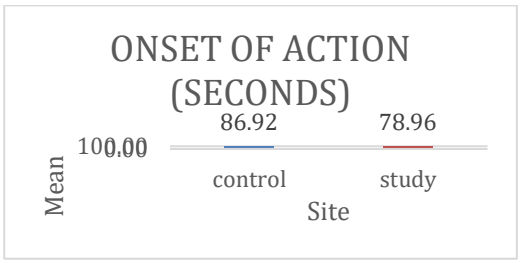
JCHR (2024) 14(1), 594-601 | ISSN:2251-6727

GRAPHS

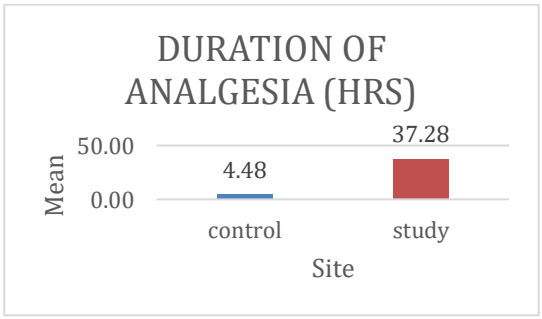
Graph I: Age & Sex Distribution



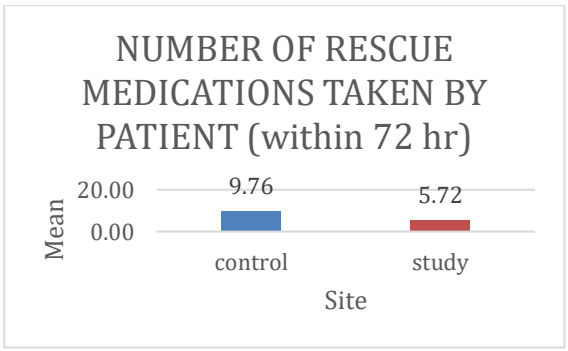
Graf II: Time of Onset of Anaesthesia:



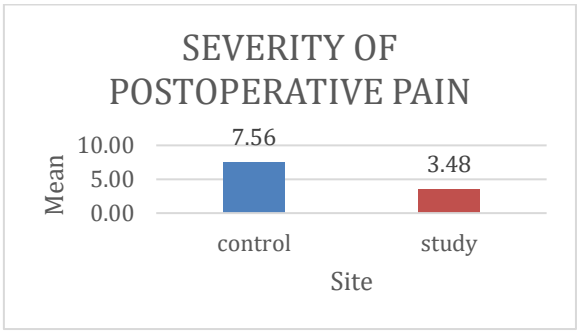
Graph III: Duration of Anaesthetic Effect:



Graph IV: Total Number of Rescue Analgesics Consumed:



Graph V: Severity of Postoperative Pain (Checked by VAS scale):



DISCUSSION

The success of the surgical procedures primarily depends upon achieving minimal postoperative pain. It forms the major cause of distress for the patients in immediate postoperative period. At present oral, intramuscular and intravenous analgesics were given for postoperative pain. Though the analgesia achieved in these methods were satisfactory, they were invasive methods and undergoes first pass metabolism.

Local anaesthetics represent some of the most widely used drugs in medicine and dentistry for the prevention and management of pain. Since 1943, routine minor oral surgical procedures are performed widely using 2% lignocaine hydrochloride with adrenaline (1:80000) and success of it relies on the efficiency of the local anaesthetic agent used, which blocks the sensation of pain by reversibly blocking nerve conduction when applied to a circumscribed area of the body. The administration of additional analgesics, and or sedatives, can be impractical, time consuming or even contraindicated. [9]

The choice of anaesthetic solution should be based on three main clinical considerations: anaesthetic potency, latency period (onset of anaesthesia) and duration of anaesthesia effect. Lignocaine is, today the ‘gold standard’ local anaesthetic agent against which all new local anaesthetics are compared. Though it possesses rapid onset of action and has reasonably good potency. [9]

Local anaesthetic has clinical effect of vasodilation to increase rate of absorption of local anaesthetic into blood, thus decreasing the duration and quality of pain control ,while increasing the anaesthetic

Journal of Chemical Health Risks

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JCHR (2024) 14(1), 594-601 | ISSN:2251-6727

blood(plasma) concentration which results faster onset of action and reduce its potential for overdose (toxic reaction).[9] However, there are several postoperative events associated with the administration of local anaesthetics like seizures, arrhythmias, cardiac arrest, and transient neuropathic symptoms, short duration of action have been reported after subcutaneous administration, oral administration, and intravascular administration.[10,11]

Over the past ten years, several studies have suggested, addition of certain opiates to the local anaesthetic used for block anaesthesia may provide effective and prolonged postoperative analgesia. Presence of opioid receptors in peripheral nervous system offers the possibility of providing postoperative analgesia in ambulatory surgical patients.[12] Evidence speculated that the peripheral administration of opioids provides stronger and long lasting analgesia with a lower dose of opioid and without central side effects such as respiratory depression, nausea, vomiting, and pruritus. A number of trials have examined the peripheral analgesic effect of opioids in a variety of surgical setting. [12,13,14,15]

For that several adjuvants like, magnesium, bupivacaine, dexamethasone has been used along with local anaesthesia to prolong the duration of anaesthesia and to do away with post-operative analgesics.[66] Local anaesthetics with an extended duration of action, good analgesia, and low toxicity is an optimal choice. Buprenorphine has high analgesic potential, good safety profile, ease of opioids switches and reversibility by μ- antagonist. The ease of delivery along with the local anaesthetic avoids additional punctures because of that it's a better choice as an adjuvant to prolong postoperative analgesia.

Buprenorphine is a semisynthetic lipophilic opioid which have anti hyperalgesia properties, for prevention and reduction of central sensitization. It has been used as an analgesic in the postoperative period for the treatment of moderate-to-severe pain. Its high affinity for the μ receptor along with its slow dissociation from the receptor has led to new challenges in buprenorphine maintenance therapy. It has the typical side effects shown by all opioids including nausea, vomiting, dizziness, constipation and headache. As with all other strong opioids, buprenorphine produces respiratory depression. In contrast with fentanyl and morphine, a ceiling effect on respiratory depression, but not on analgesia over a dose range of 0.05 to 0.6mg.[16,17,13,15,18] Buprenorphine shows analgesic effects, but no respiratory depression, at doses up to 10mg.

Buprenorphine is an effective analgesic with a potency at least 30 times that of morphine. The accepted range for buprenorphine analgesic effects is 0.1–10 mg. The onset of action for I. v or I.m route is 5 to 15 mints and 15 to 45 mints for the sublingual route. Buprenorphine has been used successfully via the epidural route without significant respiratory depression and with good analgesia [13,15,19]

The present clinical split mouth comparative study was carried out in 25 patients who required surgical removal of impacted mandibular third molar to evaluate role of buprenorphine hydrochloride as post-operative analgesia after surgical removal of impacted lower third molar surgery. Postoperative duration of analgesia, severity of postoperative pain, number of rescue analgesic consumed were the parameters that were assessed on 2hrs, 24hrs, 36hr ,48hr, 72hr by using VAS scale and marking on self-assessment form was done which coincides with other studies in different type of regional anaesthesia. [2,3,5,7,20,21,22,23] Onset of anaesthesia was recorded by using needle prick test.

The time of onset of anaesthesia was calculated from the point of retrieval of needle after injection, to the time of achieving objective signs of anaesthesia instead of subjective symptoms, for the sake of convenience and accuracy. In our study, the mean time of onset of anaesthesia for (control group) was 86.92 (SD:18.51) versus 78.96 (SD: 11.61) for study group. There was no significant difference in time of onset between two group ($p < 0.075$). Thus the addition of buprenorphine to the local anaesthetics had no effects on onset of anaesthesia .[2,3,7]

In our study, the mean duration of analgesia for control group was 4.48 (SD: 1.60) versus 37.28 (SD: 22.07) for study group). Statistically significant differences were observed between two groups (P=0.000) Thus the present study shows longer duration of analgesia up to 36 hr which is significant to other studies [2,3,5,7,20,21,22,23] and longer than control group.in contrast to these,

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Flory et al. found no differences in duration of analgesia

Severity of postoperative pain was recorded by visual analogue scale by marking in the self-assessment form, in our study, the mean intensity of pain for control group) was (SD: 2.78) versus 7.27 (SD:1.48) for Group-II (control group). Statistically significant differences were observed between two groups ($P < 0.001$). Thus the present study shows decreased severity of pain which is significant to other studies [2,3]

Hence on the basis of the present study and as per the support of the literature, it can be stated that efficacy of 0.3mg buprenorphine added to 2%lignocaine hydrochloride injected for inferior alveolar nerve block (IANB) provides prolonged postoperative analgesia up to (36 hr), decreases the need for pain medication in postoperative period. decreased severity of pain, but statistically no significant effect on onset of action. In view of the absence of adverse effects in small group of patients, the addition of buprenorphine 0.01mg/ml of lignocaine hydrochloride for IANB in patients undergoing lower third molar surgery may be a way to provide postoperative analgesia for outpatients.

More clinical trials with larger numbers of patients are essential to further substantiate the efficacy of buprenorphine in providing postoperative pain relief when added to local anaesthetics. Also, the correlation of plasma concentrations of buprenorphine and route of administration should be an important aspects of future studies, and the absence of this is a weakness of the current one.

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