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Effect of long-acting local anesthetic infiltration in surgical wound for post-operative pain control in Zygomaticomaxillary complex fracture

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A B S T R A C T

To compare the analgesic efficacy of Bupivacaine 0.5% wound infiltration with placebo incisional infiltration in relieving postoperative pain for first twenty-four hours. This study was performed on sixty patients, of both sexes , with varied age groups. Patients underwent open reduction Internal fixation of Zygomaticomaxillary complex fractures, confined to ASA category I-II. Patients were selected by convenience sampling and were divided into two groups i.e. Group I and group II. Group I comprised of thirty patients and were infiltrated with bupivacaine 0.5% at wound margins postoperatively. Group II also comprised of thirty patients and were infiltrated with saline at wound margins postoperatively. The postoperative pain scores in both groups were low and there were no significant difference between the groups in pain scores (p=0.07) and Analgesic consumption (p=0.11). Wound infiltration with Bupivacaine 0.5% has not been shown to provide additional analgesic or outcome benefit in the setting of a comprehensive multimodal analgesic approach.

Introduction

Surgical incision leads to cell disruption and subsequent Intracellular release of phospholipids and a state of widespread inflammation depending on the degree of surgical trauma. Enzymatic action on phospholipids results in the release of prostanoids as the site of injury that sensitizes the nociceptors to mechanical stimuli (primary hyperalgesia) and also to several chemical mediators, such as prostanoids, bradykinin and nerve growth factor. The chemical mediators may be the cause of secondary hyperalgesia since continued peripheral sensitization leads to

central pain sensitization [1]. The vast number of mediators being released during this perioperative period necessitates a multitude of pharmacological agents to treat postoperative pain , as opposed to the traditional belief that opioids were the only drugs needed.

Fear of uncontrolled postsurgical pain is a major concern of patients undergoing surgery. Effective post-operative pain control is an important factor in reducing the incidence of morbidity and in promoting early mobilization and discharge from hospital [2]. Opioid analgesics with their well-known side effects continue to play a major role in managing post-operative pain after surgeries.

With the current trends of surgery moving towards minimally invasive procedures, anesthesiologists are challenged to utilize a wider armamentarium of pharmacological agents to treat postoperative pain.

As such, adjuvants to opioids are needed for postoperative pain management to reduce side effects, usually by lowering opioid dose, although some adjuvants may directly reduce side effects[3]. In addition, high doses of opioids are a safety concern primarily due to respiratory depression.

In some patients, opioids may have a long duration of action, which hinders faster recovery thereby delaying discharge. Opioids also produce a high incidence of postoperative nausea and vomiting (PONV) which exacerbates the patient's discomfort and prevents early discharge from the hospital.

Another concern is the more recent documentation of hyperalgesia with very high opioid doses, a phenomenon seen in animals [4]. In some patients, even short-term opioid use may lead to opioid-induced hyperalgesia [5]. Further, the larger the intraoperative opioid dose, the greater will be the postoperative opioid requirement [6]. Therefore, short-term tolerance to an opioid may not be due to a decrease in its efficacy (pharmacological tolerance), but rather from an enhacement in pain sensitivity (opioid-induced hyperalgesia) leading to an apparent decrease in the effectiveness of morphine[5]. Distinguishing between these two phenomena has significant implications for managing postoperative pain. If rapid escalation of opioids in the immediate postoperative period fails to provide beneficial effects, one must consider the possibility of opioid-induced hyperalgesia.

If this is the case, areduction in opioid therapy or switching to an alternative opioid (opioid rotation) may be more beneficial. Further the use of adjuvant drugs may not only contribute on an opioid-sparing effect, but may potentially result in a reduction in opioid-induced hyperalgesia. Experimental studies suggest that opioids activate both NMDA and cyclooxygenase (COX) pronociceptive systems leading to hyperalgesia [7, 8].

Adjuvants to local anesthetics are also needed, both for peripheral nerve block or wound infiltration.

Wound infiltration with a local Anesthetic for postoperative pain relief following surgeries seems to be an attractive method because of its simplicity, safety and low cost. The benefits of wound infiltration in surgeries, however, are still controversial, as a number of original articles have been published on this issue with conflicting results [9]. The aim of the present study was to evaluate the effect of wound infiltration with Bupivacaine on postoperative pain, supplemental analgesic consumption, time to first analgesic request in patients undergoing zygomaticoMaxillary complex

(ZMC) fracture surgery by using evidence from double-blind, randomized clinical trial.

Materials and Methods

After approval of the local ethics committee, 60 adult patients with different age groups (20-60 years) belonging to both sexes, ASA physical status I-II, who were undergoing open reduction internal fixation (ORIF) of Zygomaticomaxillary complex (ZMC) fracture were enrolled in this randomized, double-blinded, placebo controlled study . After written informed consent was obtained patients were randomly allocated to the two groups (group I and group II).

Exclusion criteria consisted of preoperative opioid use or dependency, peptic ulcer disease, hepatic or renal dysfunction, psychological disease, allergy to amide local anesthetics and narcotics and seizure. Both anesthetist and surgeon were blinded to the infiltration solution. Only the staff nurse knew the group and the solution to be infiltrated. The infiltration solution composition and volume described below: Group I: thirty patients were included in this group. These patients were infiltrated with injection 10 ml of Bupivacaine 0.5% at the wound margins at the end of surgery.

Group II: Thirty patients were included in this group. These patients were infiltrated with injection 10 ml of Normal saline at the wound margins at the end of surgery.

All patients were given general anesthesia after establishment of mandatory monitoring (pulse oximetry, electrocardiography and noninvasive blood pressure monitoring). Same general anesthetic technique was adopted in all the patients. After preoxygenation with 100% O2, patients were induced with fentanyl 1µg/kg; midazolam 0.04 mg/kg, propofol 2 mg/kg and cis-atracurium 0.5 mg/kg and patients were intubated. Post-operative pain management was performed with analgesic drug usage, if needed, and duration of analgesia was recorded. Intravenous morphine 10 mg bolus as analgesia drug was used if needed. Visual analogue scale (VAS) was used for estimate of pain degree in patients at 0, 2,4,6,12,24 hours after surgery. Application of VAS was explained to the patients before operation.

Collected data were analyzed using SPSS statistical package v.21. For statistical analysis of demographic data and for comparison of groups independent samples t-test and chi-square test were used.

A P Value< 0.05 was taken as statistically significant.

Results and Discussion

In this study, 60 patients were evaluated. Demographic data, vomiting and nausea, sleep quality, blood pressure and heart rate are presented in table 1. There were no significant differences between the two groups with respect of age, gender, nausea and vomiting, Sleep quality, blood pressure and heart rate.

The duration of analgesia, visual analogue scale (VAS) at 0, and 2,4,6,12,24 hours after surgery and morphine use for pain control in first 24 hours after surgery are presented in table2. There were no significant differences between the two groups with respect of duration of analgesia, VAS at 0, 2,4,6,12,24 hours after surgery and morphine use for pain control in first 24 hours after surgery. (Table 2, Fig.1&2)

In this context, wound infiltration with local anesthetic for post- operative pain relief could be an attractive method because of the

apparent simplicity, safety and low cost that in theory may improve early postoperative pain control and minimize the need for opioids, thereby reducing the well-known opioid adverse effects.

In a recent qualitative systematic review of 9 appropriately randomized and doubles – blinded trials by M. Kjaergaard et al. aimed at evaluating the effect of infiltration of the surgical wound with local anesthetics during lumber spine surgery [9]. Only three out of the 9 comparisons found the infiltration of the wound with local anesthetics to cause a significant reduction in pain scores. The reduction in pain scores was rather transient and typically occurred in the first postoperative hours [10, 11]. Five of 9 comparisons found a 24-h reduction in supplemental opioid consumption averaging from 2.5 mg to approximately 15 mg of morphine, when infiltration with local anesthetics was made. Furthermore, the few observations of time to first analgesic request in most cases showed clinically irrelevant prolongation with local anesthetics. These findings correlate to an only minor reduction in pain score.

The variation in doses and volumes of local anesthetics used the difference in type of pain scores, the suboptimal evaluation of side effect and the difference in surgical techniques among the nine included studies may influence the interpretation of the results and complicate this systematic review analyses.

In another systematic review by D. Mccarthy et al. 10 randomized controlled trials, that they had investigated the use of intraoperative local anesthetic infiltration for postoperative pain management following total hip arthroplasty (THA)[12].

Kerr and kohan published a case series of 325 patients who were given intra-and periarticular infiltration for postoperative analgesia following THA [13]. The injection mixture consisted of ropivacaine, ketorolac, and epinephrine. The volume used for THA was 150- 200 ml. The patients were subsequently given a bolus of 50 ml of the mixture at 15 to 20 hours postoperatively via an intra- articular catheter that was sited during the surgery. The authors reported that pain scores were generally satisfactory and that two thirds of patients did not require morphine during the postoperative period.

Parvataneni et al. investigated the use of local anesthetic as part of a multimodal pain protocol following THA [14]. A mixture containing bupivacaine, epinephrine, morphine, methyl prednisolone and cefuroxime in a volume of 75-115 ml was used for infiltration. The control patients received intravenous PCA (patient-controlled analgesia) morphine. Lower pain scores and a shorter length of stay were reported in the THA patients who received infiltration.

Bianconi used ropivacaine 200 mg (40 ml) for infiltration and followed it with an extra-articular infusion of ropivacaine 10 mg/hr. for 35 hours [15]. The control group received and extra- articular saline infusion. The LIA (local infiltration Analgesia) group reported lower pain scores at rest and movement up to 72 hours postoperatively and had lesser opioid consumption. Anders en et al. used ropivacaine plus ketorolac plus epinephrine for infiltration and followed by on the first postoperative morning, an intra- articular bolus of ropivacaine plus ketorolace plus epinephrine [16].

The LIA group reported lower pain scores from 4 hours up to two weeks postoperatively and lower opioid Consumption than control group that received placebo to saline.

Busch et al. infiltrated ropivacaine plus ketorolac plus epinephrine plus morphine [17]. Further infiltration was not given in the postoperative period. The control group received standard care with no infiltration.

The LIA group reported lower pain scores on movement and lower opioid consumption in the first 24 hours.

Andersen et al. investigated the analgesic effect of wound infiltration (intra operative bolus plus top- up via catheter at 8 hours post operatively) versus epidural analgesia in patients undergoing THA [18]. The patients who received LIA had reduced opioid consumption and length of hospital stay and improved mobilization. Interestingly the LIA group reported significantly lower VAS for pain at both rest and movement from 20 to 96 hours postoperatively, after active pain treatment had ended (20 hours postoperatively).

Specht et al. Compared and LIA regimen of intraoperative ropivacaine, epinephrine and ketorolac infiltration followed by an intra-articular bolus at 10 and 22 hours postoperatively versus a regimen of intra operative LIA as above followed by a postoperative intra- articular saline bolus in 60 patients undergoing THA [19]. They found no difference in pain scores or opioid consumption between the two groups and a non-significant trend to shorter hospital stay in the intervention group. Andersen et al. investigated the analgesic efficacy of the LIA technique by comparing its use versus placebo in 12 patients undergoing bilateral THA [20]. In this study all patients received intra- operative infiltration of a ropvacaine – epinephrine solution to one hip and 0.9% saline to the other.

Supplementary boluses of the solutions used were administered at 8 and 24 hours postoperatively. All patients had a multimodal analgesic regimen (gabapentin celecoxib and acetaminophen) commenced preoperatively. The authors reported that postoperative pain scores were low and similar between the hip given ropivacaine and that given saline. They concluded that they could not therefore recommend the LIA technique in addition to the multi- modal approach. Lunn et al. compared the use of LIA (ropivacaine with epinephrine) versus placebo to infiltration with saline in 120 patients undergoing unilateral THA, again in the setting of using a preoperatively instituted multimodal analgesic regime of gabapentin, celecoxib, and acetaminophen [21]. The postoperative pain scores in both groups were low and there was no significant difference between the groups. Here again, the authors concluded that they could not recommend LIA as being superior to a multimodal approach. These two studies used only local anesthetic with epinephrine for the LIA. Therefore the possibly confounding effect of ketorolac or another NSAID in the infiltration mixture being responsible for the analgesic benefit with LIA was removed. In both of these studies the authors asserted that the LIA technique may not have a clinically relevant effect when combined with a multimodal analgesic approach and therefore was not recommended. The difference in outcome between the aforementioned trials advocating LIA and these two appears to be related to the use of a comprehensive multimodal analgesic regimen which seems to be as effective as the LIA technique.

Our study compared the use of LIA (only bupivacaine 0/5%) versus placebo infiltration with saline in 60 patients undergoing ORIF of zygomaticomaxillary complex fracture in the setting of using preoperatively instituted multimodal analgesic regime of ketorolac, Acetaminophen and dexamethasone.

Table.1 Background parameters in the two study groups

variables	Bupivacaine group (I) (n=30)	Control group(II) (n=30)	P Value
Age (year)	34.03±11.63	30.66±11.24	0.25
Gender (male/female)	25/5	26/4	1
Vomiting & nausea (No/Yes)	29/1	29/1	1
Sleep quality (good/moderate/bad)	21/7/2	25/5/0	0.26
Sistolic blood pressure	122.36±13.37	123.53±11.24	0.71
Diastolic blood pressure	76.06±12.89	73.40±13.21	0.43
Heart rate	79.30±10.85	78.83±11.01	0.86

Table.2 Clinical parameters in the two study groups

variables	Bupivacaine group (I) (n=30)	Control group(II) (n=30)	P Value
Analgesia duration (min)	22.66±25.72	26.16±38.43	0.68
VAS at 0	5.63±3.67	6.73±2.59	0.18
VAS after 2 hours	5.43±2.35	5.03±2.76	0.54
VAS after 4 hours	4.66±2.18	3.86±2.66	0.20
VAS after 6 hour	4.03±2.25	2.69±2.35	0.07
VAS after 12 hours	2.73±2.01	1.90±2.27	0.13
VAS after 24 hours	2±1.81	2±2.54	1
Morphine use (mg) in first 24 hours after surgery	38.41±14.45	41.58±15.80	0.19

Figure.1 Pain intensity as measured with visual analog scale (VAS) scores. No Statistically significant differences were noted

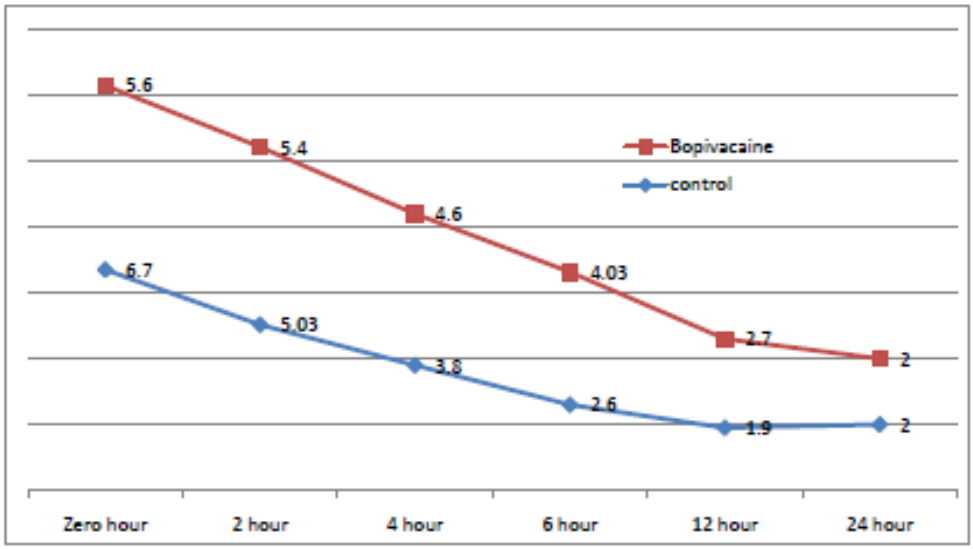
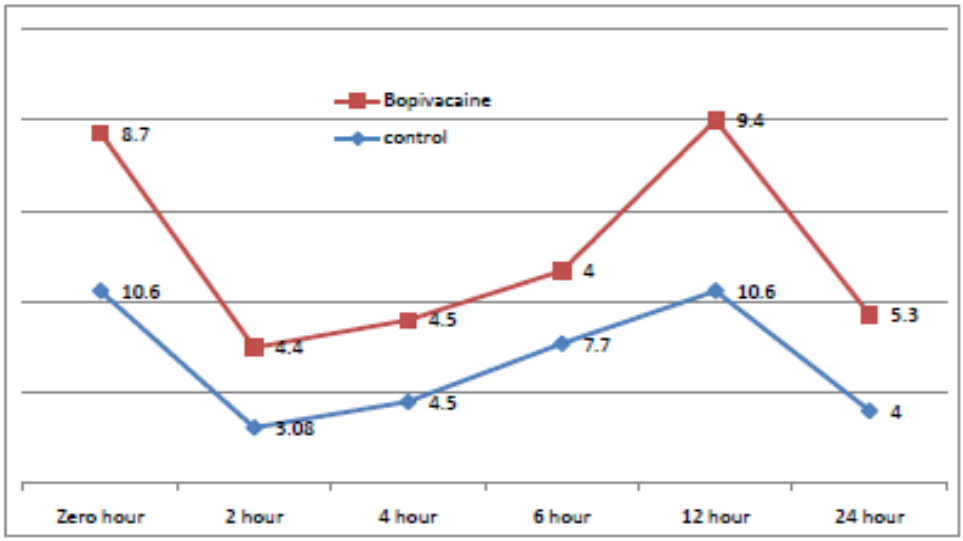


Figure.2 Cumulative patient-controlled analgesia morphine consumption. Statistically significant differences were not noted at all-time points



The postoperative pain scores in both groups were low and there was no significant difference between the groups (p=0.07).

The causes of different outcomes between the aforementioned trials (13-19) and our study are described below. First, in our study was used only local anesthetic (Bupivacaine 0/5%) for the LIA. Therefore another analgesic agents such as ketorolac or another NSAIDs that being responsible for the analgesic benefit with LIA, was removed. Second, further infiltration was not given in the postoperative period. Third, in our study, All patients had a multimodal analgesic regimen (acetaminophen, ketorolac and dexamethasone) commenced preoperatively.

Multimodal analgesic is achieved by combining different analgesics that act by different mechanisms and at different sites in the nervous system, resulting in additive or synergistic analgesia with lowered adverse effect of sole administration of individual analgesics [22].

Local infiltration analgesia (LIA) is an analgesic technique that has gained popularity since it was first brought to widespread attention by kerr and kohan in 2008. The technique involves the infiltration of a large volume dilute solution of a long – acting local anesthetic agent, often with adjuvants (e.g., epinephrine, ketorolac, an opioid), throughout the wound at the time of surgery. The analgesic effect duration can then be prolonged by the placement of a catheter to the surgical site for postoperative administration of further local anesthetic. The technique has been adopted for use for postoperative analgesia following arrange of surgical procedures (orthopedic, general, gynecological and breast surgeries) [12].

The local anesthetic used most often in published work so far is ropivacaine, likely chosen for its reduced cardiotoxicity in comparison to bupivacaine as well as for its intrinsic vasoconstrictor properties [23, 24].

The LIA technique has been reported to be easy to perform effectively and appears to be safe. Whether or not it provides the most effective analgesia following ORIF of ZMC

fractures has been questioned. In addition, it doesn't appear to be of value when used in addition to a perioperative multimodal analgesia regimen. However it may have a role in certain subset of patients such as those who are intolerant of or unsuitable for multimodal regimen referred to above. Patients who have chronic pain conditions or are habitual opioid users may benefit from the administration of LIA; however these patients are generally not included in studies of postoperative analgesia, and therefore data is locking.

Conclusion

In conclusion, the existing data regarding the use of local infiltration analgesia following ORIF of ZMC fractures consists of the results from a relatively of small sized clinical trial. The LIA technique has been shown to be an effective analgesic method. It has been proven to be superior to no infiltration, placebo saline infiltration and, in one study, epidural analgesia. It has not been shown to provide additional analgesic or outcome benefit in the setting of a comprehensive multimodal analgesic approach but can be regarded as an effective analgesic method following surgeries, and consideration should be given to its use by the surgeon and the anesthetist in the planning of the analgesic management strategy for surgical procedures where a comprehensive multimodal analgesic regimen was not used.

Research involving Human Participants

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent

Informed consent was obtained from all individual participants included in the study.

Ethical standard statement

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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