

Additional pre-extubation local anaesthetic application to improve the postoperative course in orthognathic surgery: a randomised controlled trial

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Abstract

A clinical trial was performed to assess the analgesic efficacy of adding ropivacaine pre-extubation for pain management after bimaxillary osteotomy. Forty-eight patients were assigned to receive general anaesthesia followed by either a single pre-incisional infiltration with lidocaine (control group, n=24) or the same preincisional infiltration with lidocaine and an additional second infiltration with ropivacaine before awakening (test group, n=24). Postoperative pain was assessed subjectively using a visual analogue scale and objectively based on the frequency of postoperative rescue opioid consumption. The dose of opioids (methadone) consumed and frequency of postoperative-nausea-vomiting were also recorded. Patients who received the two infiltrations of local anaesthetic had better results in terms of lesser pain during the first 8 hours postoperative ($P<0.001$ at 2 and 4 hours; $P=0.028$ at 8 h), a lesser need for rescue opioids ($P=0.020$) and lower doses of rescue opioids ($P=0.011$), and consequently a lesser incidence of postoperative-nausea-vomiting (0-4 hours postoperative, $P<0.03$). The results obtained suggest that the infiltration of an additional dose of local anaesthetic is a simple strategy for reducing pain perception and opioid use, and for ensuring greater patient comfort after bimaxillary osteotomy.

Orthognathic surgery seeks to correct dentofacial deformities for both functional and aesthetic reasons, and the control of patient pain in the perioperative period is of crucial importance.

Bimaxillary orthognathic surgery is conducted under general anaesthesia, although isolated peripheral nerve blocks are also widely used.⁽¹⁻³⁾ The practice of local anaesthesia provides multimodal perioperative pain control, with effective postoperative analgesia and a minimisation of respiratory depression due to excessive opioid use.^{4, 5} In general, the choice of local anaesthetic (LA) is influenced by factors such as the onset of action, duration of action, and toxicity. A wide range of LAs have been used in maxillofacial surgery, including lidocaine and ropivacaine, among others.⁽¹⁻³⁾ Lidocaine has a faster onset of action (shorter

latency) than ropivacaine, and exerts an antiarrhythmic effect, while ropivacaine is more potent and has a longer duration of action than lidocaine, and is less cardiotoxic than other equipotent LAs such as bupivacaine or levobupivacaine.⁽⁶⁻⁸⁾ Current clinical guidelines recommend the management of postoperative pain control in a multimodal manner, including the use of Las.⁴

The present study proposes LA infiltration in two stages, before and after surgery, using two different LAs in order to optimise perioperative pain control. Specifically, the aim of this double-blind randomised controlled trial was to determine whether a second infiltration of LA pre-extubation added to a general anaesthesia regimen with pre-incisional LA infiltration, is able to further reduce postoperative pain in adult patients after bimaxillary osteotomy.

Patients and methods

A prospective, double-blind randomised controlled trial was performed between July 2019 and January 2020 in patients undergoing bimaxillary orthognathic surgery at Teknon Medical Center (TMC, Barcelona, Spain). The study was approved by the TMC Ethics Committee (registration number: RopiLido 2017.1) and has been registered at ClinicalTrials.gov (registration number: NCT03974035). Written informed consent was obtained from all participating patients before inclusion in the study. This study is reported in accordance with the Consolidated Standards of Reporting Trials (CONSORT) statement.

Randomisation and blinding

A statistician not participating in any other way in the study generated a 1:1 randomisation table for patient allocation. Then, sealed opaque envelopes containing patient allocation were prepared: group 1, control (no additional LA application) and group 2, test group (additional LA application, performed pre-extubation). The anaesthesiologist opened the envelope in the operating room after the administration of general anaesthesia and nasotracheal intubation, making sure that the patient remained blinded to the group allocation. Nurses in the postanesthesia care unit (PACU) and in the inpatient ward who recorded the patient pain scores and administered the opioids after the operation were also blinded to the group allocation. Therefore, only the anaesthesiologists and surgeons in the operating room were not blinded, while the nurses, research assistants, and patients were all blinded to the group allocation.

Study subjects

The study inclusion criterion was patients undergoing elective bimaxillary orthognathic surgery. The following exclusion criteria were applied: patient refusal to participate, patients undergoing single-jaw orthognathic surgery, patients undergoing bimaxillary orthognathic surgery together with another surgical procedure (e.g., rhinoplasty, blepharoplasty), age < 18 years, reoperations, urgent surgery, allergy to LAs, anti-inflammatory medications, or

opioids, or any contraindication to adjuvant drug treatments, and an American Society of Anesthesiologists (ASA) physical status score ≥ 3 .

Study outcomes

The primary outcome assessed in this study was postoperative pain evaluated with a visual analogue scale (VAS). Secondary outcomes were the consumption and dose of rescue analgesia (opioids) and the frequency of postoperative nausea and vomiting (PONV).

Surgery and anaesthetic management

The patients were received in the surgical area where premedication was administered, anaesthetic induction was performed, and anaesthetic maintenance was started.

Following nasal intubation, LA was applied in all patients (control and test groups). The surgeon performed preincisional LA application with lidocaine and adrenaline; a total of 50 ml of the following pre-incisional mixture was administered: 0.5 amp adrenaline 1mg/ml and 1 amp 10 ml lidocaine 2% made up to 100 ml with physiological saline solution. This was administered at the intraoral and intranasal submucosal level in the upper and lower maxilla in order to block the terminal branches of the maxillary and mandibular nerves (superior alveolar, inferior alveolar, lingual, and buccal nerve block sites). Specifically, 15 ml was administered in the maxilla at the intraoral level, 15 ml in the maxilla at the intranasal level, and 20 ml at the mandibular level.

In all cases, the orthognathic surgery consisted of mandibular osteotomy followed by maxillary osteotomy.

After surgery and pre-extubation, the surgeon repeated the same LA application in the test group patients only, to block the terminal branches of the maxillary and mandibular nerves, but using ropivacaine. A total of 20 ml of the following mixture was administered: 1 amp 10 ml of ropivacaine 0.75% and 10 ml of physiological saline solution. Specifically, 8 ml was administered in the maxilla at the intraoral level, 4 ml at the intranasal level, and 8 ml at the mandibular level.

The patients were extubated in the operating room and then transferred to the PACU for the first two postoperative hours, and were then moved to the ward for the next 2-18 h, for continued postoperative care.

Study variables

The following parameters were recorded: demographic (age, sex) and anthropometric data (weight in kilograms, height in centimetres), comorbidities, anaesthetic risk (ASA score), and any complications of LA administration.

Postoperative pain intensity was scored using a 0-10 VAS (0= no pain and 10= worst pain imaginable). Pain was evaluated every 15 min during the first 2 h after

surgery in the PACU. Afterwards, the patients were transferred to the ward, where pain intensity was assessed with the VAS at 4, 8, and 18 h post-surgery.

As an objective measure of pain intensity, data on the use and dosage of postoperative rescue opioids were recorded in the PACU (first 2 h after surgery) and in the ward (up to 18 h postoperatively). According to the protocol at the study centre, a VAS score > 3 in the postoperative period is considered to indicate insufficient pain control, and rescue analgesia is provided. The initial rescue analgesia comprises anti-inflammatory medication in the form of metamizole 2 g (intravenous) in the PACU and then paracetamol 1 g/8 h plus dexketoprofen 50mg/8 h (intravenous) in the ward. If the pain fails to subside, then an opioid (methadone) is given: intravenous methadone 2 mg in the PACU and subcutaneous methadone 5 mg in the patient ward.

Moreover, as opioids induce PONV, the incidence of the latter was also recorded at 2, 4, 8, and 18 h post-surgery.

Statistical analysis

The study protocol included the calculation of the sample size and statistical power.

The assessment of the analgesic efficacy of the two LA applications was based on postoperative pain scored with the VAS during the first two postoperative hours. This was regarded as the primary response from which to estimate the required sample size. The sample size depended directly upon the minimum clinically relevant difference in mean pain scores between the two groups at 2 h post-surgery. Table 1 provides sample sizes for different minimum difference values with a power of 80% and a significance level of 0.05 (PASS 2008; NCSS LLC, Kaysville, UT, USA). As standard deviations between 0.84 and 1.6 have been reported in studies on different groups of LAs and at measurement time-points closer to 2 h, ^{9, 10} this level of variability was assumed in the present study (± 1.03). For a larger clinically relevant pain score with a minimum difference in score of 1 (VAS score 5 in one group versus VAS score 6 in the other), a total sample of 48 cases (24 per group) would be needed under the same previous conditions. With the sample size finally included in the study (48 patients), a power of 80% was reached to detect a VAS difference of 1.03 points (large effect size $d=0.83$) with a t-test for the comparison of independent groups.

A descriptive analysis was performed with the calculation of mean, standard deviation, median, and interquartile range values for the continuous variables and absolute and relative frequencies for the categorical variables. The Kolmogorov-Smirnov test revealed significant deviations from the normal distribution for most of the response variables. Hence the objectives of the study were addressed from a non-parametric approach.

The inferential analysis consisted of the following: (1) the Mann-Whitney nonparametric test to compare the distributions of pain VAS scores and methadone dose between the two study groups; (2) the χ^2 test of independence

to compare the frequency of methadone use and of PONV between the two groups (Fisher's exact test was also used when expected values in the frequency tables were very small); (3) the Brunner-Langer nonparametric model to compare the longitudinal data for pain and PONV across the different time-points of assessment; the ANOVA-type statistic (ATS) was calculated to evaluate the pattern of the changes in these variables over time.

The level of statistical significance was set at 5% ($\alpha=0.05$). IBM SPSS Statistics for Windows version 22.0 (IBM Corp., Armonk, NY, USA) was used for the statistical analyses.

Results

The CONSORT flowchart corresponding to patient selection and dropouts is shown in Fig. 1. A total of 48 patients with completed evaluations of the primary outcome were included in the study (24 in each group). There were 29 men and 19 women, with a mean age of 32.1 ± 10.6 years.

There were no significant differences in the baseline demographic characteristics between the control and test groups (Supplementary material Table S1).

Regarding the surgery, all procedures comprised bimaxillary surgery without complementary treatments.

The change in postoperative pain scores over time is reported in Table 2. At all time-points up to 8 h after surgery, the pain score in the test group was significantly lower than that in the control group (2 h and 4 h, $P < 0.001$; 8 h, $P = 0.028$). At 18 h, the pain scores were similar in the two groups. The pattern of pain behaviour over time differed between the groups ($P < 0.001$): while the control group presented a high level of pain with a gradual reduction in the pain score over time, the test group showed lower pain scores from the start that remained more stable.

Regarding the use of methadone during admission to the PACU (administered when the patient had a VAS score > 3), 70.8% of the control patients required this medication, compared to only 37.5% in the test group ($P = 0.020$). During admission to the ward (from 4 to 18 h after surgery), the frequencies were 29.2% and 8.3%, respectively ($P = 0.137$). Regarding the dose of methadone consumed, the median dose in the PACU was 2.5 mg in the control group and 0 mg in the test group ($P = 0.011$), while the median dose in the ward was 0 mg in both groups (Table 3).

The results for PONV are shown in Table 4. The incidence of PONV was significantly higher in the control group during the 0-2 h ($P = 0.001$) and 2-4 h ($P = 0.029$) postoperative time periods. Moreover, the incidence of PONV over time varied significantly between the two groups ($P = 0.012$).

No complications related to the preincisional or pre-extubation LA application were reported.

Discussion

Despite advances in surgical techniques and anaesthetic management, patients who undergo orthognathic surgery continue to experience postoperative pain of moderate to severe intensity.¹¹ The intravenous administration of opioids is not only useful for intraoperative nociceptive stimulus control, but is also commonly used in bimaxillary orthognathic surgery to control postoperative pain. However, this increases the risk of PONV, with greater patient dissatisfaction and prolongation of the hospital stay.^{4, 5} It is important to highlight the need to reduce PONV, because such a reduction would also reduce the risk of bronchial aspiration in patients with postoperative intermaxillary fixation and decrease postoperative oedema. For this reason, current clinical guidelines recommend the management of postoperative pain control in a multimodal way,¹² including the use of LAs in infiltration of the surgical field and infiltration of the terminal nerve branches, as well as ultrasound-guided nerve blocks.

The results of this study showed the benefits of adding ropivacaine pre-extubation for acute postoperative pain management after bimaxillary orthognathic surgery, with lower pain VAS scores, reduced consumption of opioids, and lesser PONV in patients receiving this additional LA. Recently, Kumar et al.¹³ published the results of a study on supplemental LA application in a smaller sample of patients undergoing single-jaw mandibular orthognathic surgeries, and reported no evidence of statistically significant benefits. Their trial was well conducted and described. However, the patients underwent only mandibular osteotomy, a surgery with a potentially lower proinflammatory response and less release of cytokines than bimaxillary orthognathic surgery.^{14, 15} In addition, the volumes of LA used were smaller (2 ml of 0.5% bupivacaine) when compared to the volumes used in the present study and by other authors who have reported good results for regional nerve blocks before orthognathic surgery.^{16, 17}

This study has a number of strengths and limitations that need to be considered. Firstly, blinding of the anaesthesiologist and surgeon was infeasible; however, the patients and nurses (postoperative care unit and ward nurses) were all blinded to the group allocation, which adds consistency to the study. Secondly, dosing of the remifentanyl infusion by the anaesthesia care team is based on standard criteria such as haemodynamic responses. In this regard, it would have been better if such dosing had also relied on data provided by nociception monitors. Thirdly, the terminal branches of both the maxillary and mandibular nerves are involved in the perioperative pain experienced by patients undergoing bimaxillary orthognathic surgery. In this study, while the maxillary region was anaesthetised by infiltration of the terminal branches of the maxillary nerve (superior alveolar nerves), the mandibular region was anaesthetised by infiltration of the terminal branches of the mandibular nerve (inferior alveolar, lingual, and buccal nerves). These blocks have different effects and durations. In addition, there are anatomical variants of these nerves with a non-negligible incidence,^{18, 19} which could have affected the results, since the LA injection was

based on anatomical references and was not guided by ultrasound. Therefore, a new study could be considered in which the maxillary and mandibular nerves are blocked under ultrasound guidance before they issue their multiple branches in order to standardise the LA injections. This is the main limitation of the study, along with the lack of exact matching of the types of surgery and durations of surgery between the patients, which is not possible in practice.

In conclusion, based on the favourable outcomes obtained, the researchers recommend this technique of additional pre-extubation application of local anaesthetic.

Ethical approval

This trial was approved by the Ethics Committee of Quiron Teknon Medical Center (Registration no.: RopiLido 2017.1).

Patient consent

Patient consent was requested to all patients.

Trial registration

Clinicaltrials.gov identifier: NCT03974035. Principal investigator: Gloria Molins. Date of registration: June 2019.

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None.

Competing interests

None.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.ijom.2023.05.010.

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Table 1. Total sample size necessary to detect the difference in mean pain score and the statistical power reached, assuming a standard deviation of ± 1.25 for a confidence level of 95% and an independent samples t-test.

Minimum difference to detect in pain VAS score	Effect size (d)	Power reached		
		70%	80%	90%
0.5	0.4 (medium)	158	200	266
1	0.8 (large)	42	52	68
1.03	0.83 (large)	38	48	64
1.5	1.2 (very large)	20	24	32

VAS, visual analogue scale.

Table 2. Change in pain VAS score during follow-up according to the study group: control (no additional local anaesthetic application) and test (additional pre-extubation local anaesthetic application); median (range) values.

Group	Time post-surgery				<i>P</i> -value ^a (BL)
	2h	4h	8h	18h	
Control	5.0 (0–10)	4.5 (0–9)	4.0 (0–7)	3.0 (0–6)	< 0.001*
Test	1.0 (0–7)	2.0 (0–5)	2.0 (0–7)	2.0 (0–5)	
<i>P</i> -value ^b (MW)	< 0.001*	< 0.001*	0.028*	0.127	

ATS, ANOVA-type statistic; BL, Brunner–Langer model; MW, Mann–Whitney U-test; VAS, visual analogue scale. **P* < 0.05, significant.

^aATS test of the Brunner–Langer model for the difference in the pattern of change in pain VAS score between the two groups.

^bMann–Whitney U-test for the difference in pain VAS score between the groups at each given time point.

Table 3. Methadone use in the PACU and ward according to the study group: control (no additional local anaesthetic application) and test (additional pre-extubation local anaesthetic application); percentage of patients requiring methadone and median (range) dose.

		Control	Test	<i>P</i> -value ^a
PACU	% patients	70.8%	37.5%	0.020*
	Dose (mg)	2.5 (0-8)	0 (0-6)	0.011*
Ward	% patients	29.2%	8.3%	0.137
	Dose (mg)	0 (0-5)	0 (0-5)	0.067

ATS, ANOVA-type statistic; BL, Brunner–Langer model; PONV, postoperative nausea and vomiting; VAS, visual analogue scale. **P* < 0.05, significant.

^aATS test of the Brunner–Langer model for the difference in the pattern of change in PONV incidence between the two groups.

^b χ^2 test or Fisher's exact test for the difference in PONV incidence between the groups at each given time point.

Table 4. Change in the incidence of PONV during follow-up according to the study group: control (no additional local anaesthetic application) and test (additional pre-extubation local anaesthetic application); rate of affected patients.

Group	Time post-surgery				<i>P</i> -value ^a (BL)
	0-2h	2-4h	4-8h	8-18h	
Control	50%	45.8%	20.8%	8.3%	0.012*
Test	8.3%	16.7%	16.7%	0.0%	
<i>P</i> -value ^b (MW)	0.001*	0.029*	1.000*	0.489	

ATS, ANOVA-type statistic; BL, Brunner–Langer model; PONV, postoperative nausea and vomiting; VAS, visual analogue scale. **P* < 0.05, significant.

^aATS test of the Brunner–Langer model for the difference in the pattern of change in PONV incidence between the two groups.

^b χ^2 test or Fisher's exact test for the difference in PONV incidence between the groups at each given time point.

Fig. 1. CONSORT diagram of patient recruitment.

