Original Article

Analgesic efficacy of the inferior alveolar nerve block for maxillofacial cancer surgery under general anaesthesia - A randomised controlled study

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ABSTRACT

Background and Aims: Mandibular resection during maxillofacial cancer surgery evokes a strong sympathetic response requiring high doses of opioids. We studied the effect of the inferior alveolar nerve block (IANB) for analgesia in maxillofacial cancer surgeries. **Methods:** This randomised controlled study was conducted over five months in a tertiary care cancer hospital following Institutional Ethics approval and trial registration. Fifty consenting adult patients belonging to the American Society of Anesthesiologists (ASA) physical status I and II requiring maxillofacial cancer surgery with unilateral mandibular resection were recruited. Twenty-five patients in the study arm received ipsilateral IANB; a mock injection was given to the control group. Fentanyl requirement and haemodynamic parameters during primary tumour excision were the primary and secondary endpoints. Student's *t*-test was applied to compare primary and secondary endpoints. **Results:** Forty-nine patients completed the study. Both arms were comparable with respect to age, gender distribution, ASA physical status and baseline heart rate (HR) and blood pressure (BP). The mean (standard deviation) intravenous fentanyl requirement during primary tumour excision in the IANB arm was 70(32) μg, significantly lower than 183(48) μg in the control arm, $P < 0.001$. The mean maximum HR during primary tumour excision was 82 and 99 per minute in the IANB and control arms, respectively ($P < 0.001$) whereas the maximum mean BP was 88 and 101 mm Hg, respectively ($P < 0.001$). **Conclusion:** IANB significantly reduced intraoperative fentanyl requirement and caused fewer haemodynamic changes during maxillofacial cancer surgery requiring unilateral mandibular excision.

Key words: Analgesia, inferior alveolar nerve block, mandibular, maxillofacial cancer surgery, opioid, pain

INTRODUCTION

Maxillofacial surgery involving mandibular resection is often needed in treating oral cancers. This radical surgery is often associated with a severe sympathetic response.[1] Control of the sympathetic response usually requires high dose of opioids and occasional use of hypotensive agents. The perioperative adverse effects of opioids, such as respiratory depression and postoperative nausea and vomiting, are well known. More recently, there is also considerable interest in the role of opioids in cancer recurrence[2,3] and postoperative hyperalgesia.[4,5]

The inferior alveolar nerve provides sensory innervation to the body of the mandible and lower portion of the ramus, mandibular teeth, the floor of the mouth, the anterior two-thirds of the tongue, gingivae on the

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lingual/labial surface of the mandible, mucosa, skin of the lower lip and chin. The inferior alveolar nerve block (IANB) is a safe peripheral nerve block used for mandibular dental extractions.[6,7] We hypothesised that IANB would reduce the pain and stimulation associated with maxillofacial cancer surgery involving mandibular excision. This study aimed to investigate the effect of this block on intraoperative analgesia by comparing the amount of fentanyl used in the IANB arm versus the control arm during tumour excision. The secondary objectives were to compare the maximum heart rate (HR) and blood pressure (BP) during primary tumour excision and the maximum change in HR and mean arterial BP from the baseline values during primary tumour removal.

METHODS

The Institutional Ethics Committee approved the trial (Vide approval number 1648 dated 4 April 2016) and registered with ClinicalTrials.gov. (https://clinicaltrials.gov/ct2/show/NCT02745288). This double-blind, randomised, controlled study was conducted over five months from June 2016 to October 2016 in a tertiary care cancer hospital. The study was carried out in accordance with the principles of the Declaration of Helsinki, 2013; written informed consent was obtained for participation in the study and use of the patient data for research and educational purposes.

All patients between 18 and 75 years of American Society of Anesthesiologists physical status (ASA PS) I and II, scheduled for maxillofacial cancer surgery requiring unilateral mandibular resection and unilateral neck dissection, were assessed for eligibility. The anatomical feasibility of performing IANB was determined by clinical assessment and computed tomography scan. Patients with surgery involving upper alveolar/maxillary resection, with body mass index (BMI) below 18 kg/m^2 and above 30 kg/m^2, allergy to the local anaesthetic agents, pregnant women and patients with preoperative pain requiring regular pain medications were excluded. Patients unable to give valid consent, like those with learning difficulties and those with uncontrolled haemodynamic status (baseline BP above 160/90 mmHg and baseline HR above 100 per minute), were also excluded from the trial.

The anaesthetic management of all patients included in the study was standardised. All patients underwent a minimum standard monitoring consisting of a pulse oximeter, electrocardiogram, capnography, non-invasive blood pressure monitoring and temperature monitoring. Anaesthesia was induced with intravenous (IV) fentanyl 2 μg/kg and propofol 2-3 mg/kg. Neuromuscular blockade was achieved with IV vecuronium bromide 0.1 mg/kg, following which the trachea was intubated with an appropriate sized nasotracheal tube. Anaesthesia was maintained with isoflurane in an air and oxygen mixture with a minimum alveolar concentration of 0.8–1.2. After anaesthesia induction and confirmation of the surgical plan, the patient was randomised by opening sequentially numbered sealed opaque envelopes prepared a priori by the Clinical Research Secretariat to ensure allocation concealment. Computer-based stratified block randomisation was used to ensure that 25 patients were allotted to the IANB arm and control arm each.

Before the start of the study, an investigator performed five IANBs under the supervision of a maxillofacial dental surgeon. After this training period, the same investigator performed all blocks in the trial. Ipsilateral IANB was performed after induction of anaesthesia, 10–30 min before commencing surgery for primary tumour excision, with full aseptic precautions after donning a sterile gown and gloves. The ipsilateral mucobuccal fold was palpated and traced to the coronoid notch. The fingertip was advanced medially across the retromandibular trigone on the internal oblique ridge. A 25G needle was inserted till the bone was felt, and a standard dose of 2 ml of bupivacaine 0.5% was injected slowly after withdrawing the needle by 1 mm, confirming negative blood aspiration.[7,8] The same procedure was followed in the control arm, but the local anaesthetic was spilt in the oral cavity. As the primary outcome was intraoperative IV fentanyl requirement, the attending anaesthesiologist was blinded by being asked to step away from the operating field during the study intervention. Therefore, the actual procedure and injection site were not visible to them, ensuring blinding to group allocation. Thus the study was patient and assessor-blinded.

BP and HR were noted before anaesthesia (baseline), at induction and 5 min intervals from the baseline till neck dissection and primary tumour excision were completed. During neck dissection and primary tumour excision, IV fentanyl was administered in 1 μg/kg boluses for intraoperative analgesia. A 15–20% rise in BP and HR over the baseline values was considered a significant haemodynamic response needing additional doses of intravenous fentanyl. In case of a persistent sympathetic response to surgery, i.e. BP and HR 15–20% above baseline, which was not controlled by a maximum dose of IV fentanyl 10 μg/kg, administration of rescue IV analgesics or anaesthetic drugs such as IV diclofenac 1 mg/kg single dose, propofol 10–20 mg boluses as required, dexmedetomidine infusion at 0.2–0.6 μg/kg/h, or infusion of IV vasoactive agents such as esmolol or nitroglycerine in titrated doses was allowed and noted. The analgesia management followed standard practice after primary tumour removal and neck dissection.

The intraoperative charts were analysed by a part of the investigation team blinded to group allocation. The amount of fentanyl used during the neck dissection and primary tumour excision was recorded. The data regarding haemodynamic parameters, use of any vasoactive drugs and complications, if any, was collected.

The primary outcome was IV fentanyl administered during primary tumour excision. The secondary outcomes were maximum HR and BP during primary tumour excision and maximum change in HR and BP from baseline during primary tumour excision.

Based on our pilot data from 30 patients, the mean (standard deviation [SD]) fentanyl requirement during primary tumour excision and neck dissection in patients undergoing maxillofacial surgery requiring unilateral mandibulectomy was 340 (101) μg. To detect a 25% reduction in fentanyl requirement in the IANB arm compared to the control arm, with 80% power and significance of 5%, the sample size calculated was 22 patients in each arm. The total sample size of 50 patients was selected, considering possible losses due to protocol violation. Statistical Package for the Social Sciences (SPSS) statistics software version 21.0 (IBM, NY, USA) was used for statistical analysis. Continuous numerical variables (duration of surgery, fentanyl requirement) are presented as mean (SD), and the intergroup differences (age, BMI) were compared using the Student's *t*-test after assessing the normality of the data. Categorical variables (gender, type of surgery and reconstruction) are presented as numbers, and inter-group differences are compared using the Chi-square test. $P < 0.05$ was considered to be statistically significant.

RESULTS

Fifty patients posted for elective unilateral mandibular resection were recruited and randomised to the study [Figure 1]. One patient had an anaphylactic reaction soon after randomisation and study procedure. The randomisation was disclosed to be the control arm, and the patient was excluded from the study due to loss of blinding and protocol violation. The reaction was attributed to gelatin infusion. The patient had an uneventful recovery. No block-related complications were seen in any patients randomised to the IANB arm.

Both arms were comparable in demographic characteristics and surgical details [Table 1]. The mean (SD) fentanyl requirement during primary tumour removal was 70(32) μg in the IANB and 183(48) μg in the control arm ($P < 0.001$). The haemodynamic parameters were more stable in the IANB arm [Table 2]. None of the patients in either arm needed additional interventions to control a severe haemodynamic response.

DISCUSSION

Our study showed that IANB significantly reduced the IV fentanyl requirement and sympathetic response during maxillofacial surgery with mandibular resection.

Most studies on nerve blocks for head and neck surgery have used IANB or mandibular nerve blocks for dental or orthognathic surgery.[8-10] The mandibular nerve block covers a larger area, but it has potentially more complications as a deep-sited block. As there is little literature on the effectiveness of nerve blocks in maxillofacial cancer surgery, we chose the IANB as it is a relatively safe, superficial and easy-to-perform

Table 1: Comparison of demographic variables and surgery-related parameters

Patient characteristics	IANB arm (*n*=25)	Control arm (*n*=24)
Age, years	47.9 (10.4)	48.2 (12.5)
Gender (male/female)	20/5	18/6
BMI (kg/m^2)	22.4 (2.5)	23.7 (3.4)
ASA PS I/II	23/2	18/6
Baseline HR (beats/min)	79.7 (7.9)	81.4 (9.3)
Baseline MAP (mm Hg)	89.7 (8.7)	83.9 (5.9)
Duration of primary tumour excision (min)	63 (21)	77 (30)
Duration of neck dissection (min)	92 (25)	91 (31)
Hemi-mandibulectomy/segmental mandibulectomy (*n*)	3/22	4/20
Type of reconstruction (*n*) Primary closure/local flap/PMMC/free flap	2/3/10/10	5/1/7/11

Date represented as Mean (SD) or numbers. IANB - Inferior Alveolar Nerve block, BMI - Body Mass Index, SD - Standard Deviation, ASA PS - American Society of Anesthesiologists Physical Status, HR - Heart Rate, MAP - Mean Arterial Pressure, PMMC - Pectoralis Major Myocutaneous Flap

Table 2: Comparison of outcome parameters

Variable	IANB arm *n*=25	Control arm *n*=24	*P*
IV fentanyl during primary excision (µg)	70 (32) (56–83)	183 (48.2) (162–203)	<0.001
IV fentanyl during neck dissection (µg)	154 (35.1) (139–168)	158 (60.2) (132–183)	0.75
Maximum HR (beats/min)	82.1 (7.4) (79–85)	99.4 (9.5) (95–103)	<0.001
Maximum MAP (mm Hg)	88.1 (6.4) (85–90)	101.2 (7.5) (98–104)	<0.001
Maximum change in HR from baseline	+2.5 (9.4) (−1.4–+6)	+18 (13.6) (+12–+23)	<0.001
Maximum change in MAP from baseline (mm Hg)	−1.6 (9.4) (−5.5–+2.3)	+17.4 (9.7) (+13–+21)	<0.001

Date presented as Mean (SD) [95% CI] or numbers. SD - Standard deviation, CI - Confidence interval, IANB - Inferior alveolar nerve block, HR - Heart rate, MAP - Mean arterial pressure, IV - intravenous

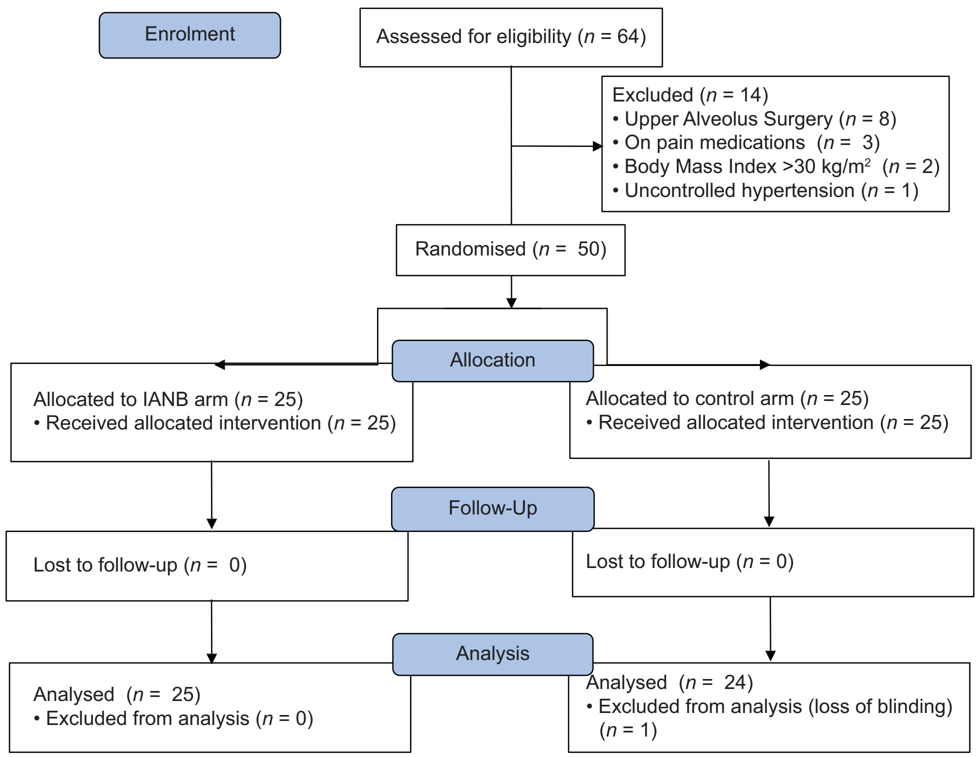

Figure 1: Patient recruitment as per consolidated standards of reporting trials (CONSORT)

block.[11] In our study, we looked at the opioid-sparing effect as a direct indicator of the effectiveness of IANB during mandibular resection. The observation that the fentanyl requirement for neck dissection before IANB was similar in the two arms adds strength to the observation that IANB was responsible for better analgesia during primary tumour excision. Chen *et al*.[9] observed lower requirement of intraoperative fentanyl, lesser use of hypotensive agents such as labetalol and reduced blood loss with maxillary and mandibular nerve blocks for maxillofacial orthognathic surgery. In our study, pharmacological agents were not required for haemodynamic management in either arm.

Most studies have looked at the sympathetic stress response to surgery and found better haemodynamic stability in patients receiving nerve blocks, similar to our research. One study measured blood catecholamine levels and demonstrated lower levels using regional nerve blocks for orthognathic surgery.[8] Though we excluded patients with poorly controlled hypertension as exaggerated intraoperative hypertension could confound results, patients with cardiovascular risk factors are likely to benefit more from regional blocks due to an attenuated sympathetic response.

The strength of our study is that this is the first time a peripheral nerve block has been studied for maxillofacial cancer surgery. The safety and effectiveness of the IANB makes it suitable to be used extensively as an intraoperative analgesic technique in cancer surgeries involving mandibular resection. However, the study has a few limitations. As IANB is associated with a failure rate of around 15%, confirming its action would have been ideal.[12-14] This would have required the block to be given preoperatively.

As neck dissection was done before the primary tumour excision, the action of the block could have worn off. Also, it would cause patient discomfort. It is possible that we had a better success rate in the block given under general anaesthesia as the failure rate data of IANB is derived from patients undergoing procedures under local anaesthesia where inadequate mouth opening and pain on injection are considered barriers to giving a satisfactory injection. We chose the standard open-mouth landmark technique for IANB as it is a much-practised technique with well-defined landmarks and a low risk of complications. We also did not study postoperative analgesia as the action of a single shot block was unlikely to extend into the postoperative period in such long-duration surgeries. Also, our patients receive long-acting opioids like buprenorphine for facilitating tolerance of the nasotracheal tube (kept *in situ* overnight) or tracheostomy tube as standard care in the post-anaesthesia care unit. We did not study the effect of the block on the incidence of chronic pain as it would be challenging to discriminate post-surgical chronic pain from post-radiation pain as radiation therapy is common in these cancers.[15] Another limitation of our study was that we did not look at the effect of the opioid-sparing technique on cancer recurrence, which has been a subject of interest in recent times.[16] However, only a large study with a long follow-up can answer this question.

CONCLUSION

The IANB significantly reduced IV fentanyl requirement and caused less haemodynamic changes during radical surgery for buccal mucosa cancers requiring unilateral mandibular excision.

Study data availability

De-identified data may be requested with reasonable justification from the authors (email to the corresponding author) and shall be shared after approval as per the authors' Institution policy.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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