

PAIN

Effect of mandibular nerve block on postoperative analgesia in patients undergoing oropharyngeal carcinoma surgery under general anaesthesia

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Background. Postoperative analgesia after oropharyngeal carcinoma surgery remains poorly studied. This study investigates the effects of mandibular nerve block (MNB) with ropivacaine 10 mg ml⁻¹ in conjunction with general anaesthesia (GA) on postoperative analgesia after partial glossectomy or transmandibular lateral pharyngectomy.

Methods. In a randomized double-blind study, 42 patients (21 in each group) received an MNB by the lateral extra-oral approach (MNB group) or a deep s.c. injection of normal saline (control group). Both groups received a standardized general anaesthetic. Postoperative analgesia included fixed dose of i.v. acetaminophen and morphine via a patient-controlled analgesia device. Consumption of morphine and supplemental analgesics and pain scores at rest were measured.

Results. The mean cumulative morphine consumption was reduced by 56 and 45% at 12 and 24 h after operation in the MNB group. The administration of analgesic rescue medications was delayed in the MNB group. The visual analogue scale (VAS) pain scores were comparable in the two groups during the first 24 h. Adequate analgesia (mean VAS ≤ 3) was observed throughout the study period in the MNB group, but only from 4 h after operation onwards in the control group. The number of patients who experienced severe pain (VAS > 7) during the first postoperative day was lower in the MNB group than in the control group (3 vs 10, respectively, $P < 0.05$).

Conclusions. In this study, MNB performed before GA for oropharyngeal carcinoma surgery improved postoperative analgesia, resulting in reduced morphine consumption at 24 h and severe pain in fewer patients.

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The management of postoperative pain after head and neck carcinoma surgery remains poorly studied. Surgery for oropharyngeal and laryngeal cancer can cause severe pain, particularly in the first hour after recovery.^{1–2} Pain relief is generally provided with an i.v. opioid delivered with a patient-controlled analgesia (PCA) system.² The use of regional analgesic techniques may provide superior analgesia compared with systemic opioids^{3–4} and may even

improve rehabilitation.⁵ Mandibular nerve blocks (MNB) performed before bilateral mandibular osteotomy decreased intra-operative opioid consumption during general anaesthesia (GA).⁶ During the removal of mandibular third molars, MNB reduced postoperative pain and analgesic requirements.^{7–8} Several case reports suggest a role for continuous MNB for pain control in patients suffering from trigeminal neuralgia,⁹ fracture of the mandible,¹⁰ or terminal orofacial

cancer.¹¹ To date, no published study has evaluated the value of MNB for control of postoperative pain after oropharyngeal cancer surgery. The aim of this prospective, double-blind, placebo-controlled study was to demonstrate that the MNB performed before GA for oropharyngeal cancer surgery improves postoperative analgesia.

Methods

Approval for the study was given by the Institutional Ethics Committee and written informed consent was obtained from all subjects. Patients undergoing lateral transmandibular pharyngectomy or partial glossectomy (PG) under GA were included in this prospective, randomized, double-blind, placebo-controlled study. Patients with severe renal or hepatic impairment, heart failure, chronic respiratory disease, contraindications to regional anaesthesia, inability to understand the use of a PCA system, and ASA status >III or age <18 yr were excluded from the study. The day before surgery, patients were familiarized with a PCA device and a standard visual analogue scale (VAS) for pain (0=no pain, 10=worst pain imaginable). All patients were pre-medicated 90 min before surgery with hydroxyzine 1.5 mg kg⁻¹ and effervescent cimetidine 400 mg orally. They also received 2 g of an i.v. aminopenicillin- β -lactamase inhibitor combination according to our current protocol for antibiotic prophylaxis. Lidocaine 2.5% plus prilocaine 2.5% cream was applied to the regional block puncture site area. Patients were then randomized into two groups to receive GA plus MNB (MNB group, $n=21$), or GA plus an s.c. injection of normal saline (control group, $n=21$). Patients were assigned to a particular technique using sealed coded envelopes.

In the anaesthetic induction room, heart rate (HR), non-arterial pressure, and oxygen saturation (Sp_{O_2}) were monitored. Propofol 0.5 mg kg⁻¹ was administered to obtain a brief period of sedation while the nerve block or placebo injection was performed. All injections were carried out by senior anaesthesiologists experienced in mandibular nerve blocks and not involved in the intra- or postoperative management and evaluation of the patients. In the MNB group, the nerve block was performed by an extra-oral lateral approach.^{12 13} A 22-gauge 50 mm needle (Stimuplex®, B-Braun Medical, Boulogne, France) was introduced from the midpoint on the inferior border of the zygomatic arch through the mandibular coronoid notch. A marker was fitted 45 mm from the tip. The needle was advanced perpendicularly to the skin until it touches the lateral pterygoid plate. The marker was then shifted downwards so it was positioned at the surface of the skin. The distance between the marker and the tip of the needle was estimated to be equal to the distance between the skin and the ovale foramen. The needle was then withdrawn, re-directed posteriorly at an angle of 60° relative to the sagittal plane and advanced until the marker contacted the skin; at that point,

the tip of the needle was expected to be at the vicinity of the foramen.¹² After a careful negative aspiration, 10 ml of ropivacaine 10 mg ml⁻¹ were injected in increments. In the control group, a deep s.c. injection of normal saline (3 ml) was administered, using a 25-gauge, 30 mm needle inserted at the same point on the inferior border of the zygomatic arch. A number of measures were taken to maintain patient blinding. A similar technique of injection for the two groups was described during the preoperative anaesthetic consultation, sedation with i.v. propofol while the block was performed, and the sensory block was not evaluated in the MNB group. Furthermore, throughout the study period and particularly during their hospital stay, the patients belonging to the two groups could not communicate and thus unblind the study group assignment by comparing the details, how the anaesthetic block had been performed.

All the patients received a target-controlled propofol infusion (4–5 μ g ml⁻¹ plasma concentration), driven by a Diprifusor® system, and a continuous infusion of remifentanyl at 0.25 μ g kg⁻¹ min⁻¹. Tracheal intubation was performed after local anaesthesia of the glottis with lidocaine 5% spray. The lungs were mechanically ventilated with a mixture of 50% oxygen and 50% nitrous oxide to maintain an end-tidal carbon dioxide pressure of 4.0–4.7 kPa. A urinary catheter was inserted in all patients. During surgery, the target concentration of propofol was set to 3 μ g ml⁻¹ and the infusion of remifentanyl was titrated according to mean arterial pressure (MAP) and HR changes to maintain the values of these parameters within 20% of the baseline values measured before anaesthesia. I.V. methylprednisolone 2 mg kg⁻¹ was administered to every patient at the start of surgery. Postoperative analgesia was started 45 min before the end of surgery by administration of i.v. morphine 0.15 mg kg⁻¹ and acetaminophen 1 g. The administration of i.v. acetaminophen 1 g was repeated six times daily for 48 h after surgery. On arrival in the post-anaesthesia care unit i.v. morphine 3 mg was given every 10 min if the pain score at rest was >4 or the ventilatory frequency was >20 breaths min⁻¹. If the VAS was ≥ 4 for 60 min after the start of morphine administration, i.v. nefopam 20 mg was administered followed by 60 mg day⁻¹ given as a continuous infusion. If necessary, i.v. tramadol 100 mg followed by 300 mg day⁻¹ given as continuous infusion was added to this. When adequate postoperative analgesia had been established, patients were given access to a PCA pump. The pump was set to deliver a 1 mg bolus of morphine i.v. with a lock-out time of 10 min and a maximum cumulative dose of 24 mg every 4 h. There was no background infusion. This PCA regimen was continued on the surgical ward for 48 h after surgery, during which time other analgesics were administered if the VAS score was ≥ 4 . Pain was evaluated by a nurse blinded to the treatment group. Nausea or vomiting was treated with i.v. ondansetron 1 mg up to 4 mg day⁻¹.

The mean infusion rates of all the anaesthetic agents were calculated, as well as the duration of surgery and

anaesthesia. VAS pain scores at rest were assessed at 30 min and at 1, 2, 4, 6, 8, 10, 12, 18, 24, 36, and 48 h after the end of anaesthesia. The consumption of morphine, nefopam, and tramadol was noted, as well as the incidence of nausea, vomiting, and pruritus. Sedation was recorded using the following scale: 0, patient fully alert; 1, patient drowsy; 2, patient asleep but responsive to verbal stimuli; 3, patient unresponsive to verbal stimuli.

Statistical analysis

Morphine consumption during the first 24 h after surgery was the primary endpoint. The number of patients studied was calculated using the results of a preliminary investigation in which we determined that for similar surgery performed under GA the mean consumption of morphine was 44.6 (SD 13) mg during the first 24 h after operation. We calculated that 21 patients would be required in each group to detect a difference of at least 30% in morphine consumption during the first 24 h after surgery with a power of 90% and $\alpha=0.05$. The Power and sample size were calculated using PowerTM program.¹⁴ Secondary endpoints included fractional consumption of morphine over 2 h postoperative time intervals, administration of analgesic rescue medications, and VAS pain scores.

Data are presented as median and percentiles for VAS scores and consumption of morphine and as mean (SD) for patient characteristics. Statistical analysis was performed using StatviewTM (Abacus Concepts Inc., Berkeley, CA, USA). χ^2 test or Fisher's exact test was used to compare the qualitative variables and the Mann–Whitney *U*-test was used to compare the two groups of patients with respect to VAS scores and consumption of morphine at each time point. A Tukey correction for multiple comparisons was applied. $P<0.05$ was considered as significant.

Post hoc analyses of the different types of surgery were performed because of concerns that different operations might cause different amounts of pain.

Results

Forty-two patients undergoing oropharyngeal surgery were included in the study. Three patients were excluded because of postoperative bleeding leading to immediate re-operation (one patient in the control group) or a protocol violation (two patients in the MNB group). These were the use of ketamine for postoperative analgesia and a change of surgical indication for a benign tumour. The two groups were similar with regard to age, weight, sex ratio, ASA physical status, duration of surgery and anaesthesia, mean infusion rate of propofol or remifentanyl, and surgical characteristics (Table 1). Blood aspiration was noted in 5 of the 19 nerve blocks performed in the MNB group (26.3%); in these cases, the needle was slowly withdrawn until no blood was aspirated and ropivacaine was injected carefully with frequent aspiration. Paraesthesia in

Table 1 Patients and surgical characteristics. Values are given as mean (SD), except for the age which is given as median (range)

Variable	MNB group (n=19)	Control group (n=20)
Age (yr)	55 (40–70)	52 (37–76)
Male to female ratio	18/1	19/1
Weight (kg)	67 (12)	66 (14)
ASA physical status II/III	12/7	16/4
TNM classification		
T1/T2	1/8	1/9
T3/T4	6/4	6/4
Transmandibular lateral pharyngectomy (TMLP)		
Partial glossectomy	4	4
Tracheostomy	19	20
Lymph node clearing	18	20
Pectoralis major flap reconstruction	6	9
Duration of surgery (min)	236 (105)	226 (78)
Duration of anaesthesia (min)	275 (91)	277 (77)
Remifentanyl ($\mu\text{g kg}^{-1} \text{min}^{-1}$)	0.19 (0.05)	0.21 (0.06)
Propofol ($\text{mg kg}^{-1} \text{min}^{-1}$)	0.11 (0.19)	0.12 (0.03)

the distribution of the mandibular nerve was observed in 6 of 19 patients (31.6%). No complications were noted in the control group. The cumulative consumption of morphine (the initial i.v. dose plus morphine from the PCA) at 24 h was lower in the MNB group [26.7 (18) mg] than in the control group [48.5 (26.3) mg], $P<0.05$. The amount of morphine given i.v. immediately after surgery was lower in the MNB group [4.8 (4.2) mg] than in the control group [7.9 (6) mg], but the difference did not reach the statistical significance. The consumption of morphine from the PCA system over each 2 h time interval was lower in the MNB group for the first 12 h after surgery. The difference was significant for the H0–H2, H2–H4, and H6–H8 time intervals (Fig. 1). At 48 h, there was no difference in the total consumption of morphine between the two groups. The sum of the initial dose plus morphine from the PCA was 51.4 (31.6) and 62.7 (35.6) mg for MNB and control groups, respectively.

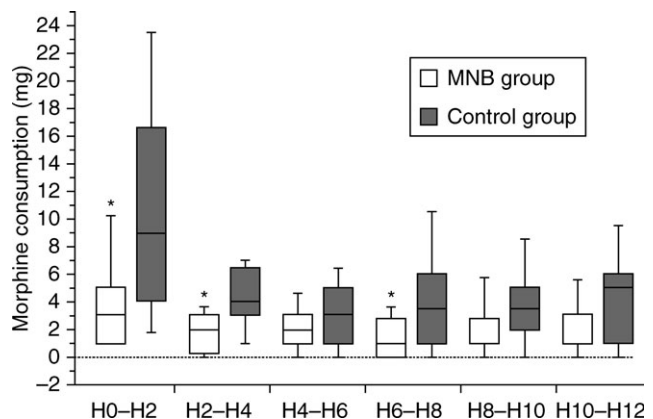


Fig 1 Morphine fractional consumption over 2 h postoperative time intervals. The box represents the 25th–75th percentiles, the dark line is the median, and the extended bars represent the 10th–90th percentiles. * $P<0.05$.

A decrease in morphine consumption at 24 h observed in the MNB group for different types of surgery was analysed separately. When only the patients with a pectoralis major flap reconstruction were considered, the morphine consumption in the MNB group was 23.8 (21) mg ($n=6$) compared with 47.3 (13.9) mg ($n=9$) in the control group ($P=0.045$). If the pectoralis major flap reconstruction patients were excluded, morphine consumption in the MNB group was [28.1 (17.4) mg, $n=13$] compared with [49.4 (34) mg, $n=11$] in the control group. This difference was not statistically significant ($P=0.13$). For the lateral pharyngectomy patients, the morphine consumption at 24 h was 25 (18.3) and 50.8 (26.3) mg in the MNB ($n=15$) and in the control ($n=16$) groups, respectively, ($P=0.01$). There were only four PG patients in each group. For this operation, the reduction in morphine consumption was not significant being 32.2 (18.4) vs 39.2 (17 mg) in the MNB vs control groups, respectively.

Additional nefopam was administered to seven patients in the control group and three in the MNB group. Tramadol was given to two patients in the control group and no patients in the MNB group. Overall, three patients in the MNB group required supplemental analgesics vs seven in the control group. This difference was not significant. Administration of rescue medications was significantly delayed in the MNB group [520 (385) min] compared with the control group [120 (63) min] ($P<0.05$). None was administered after failure of morphine titration. The VAS pain scores were statistically comparable in the two groups during the first 24 h (Fig. 2). The number of patients who experienced severe pain (VAS >7) during the first day after operation was lower in the MNB group than in the control group (3 vs 10, respectively, $P<0.05$). The two groups were similar with respect to the incidence of postoperative nausea and vomiting (one patient in each group requiring ondansetron), pruritus or sedation score (data not shown).

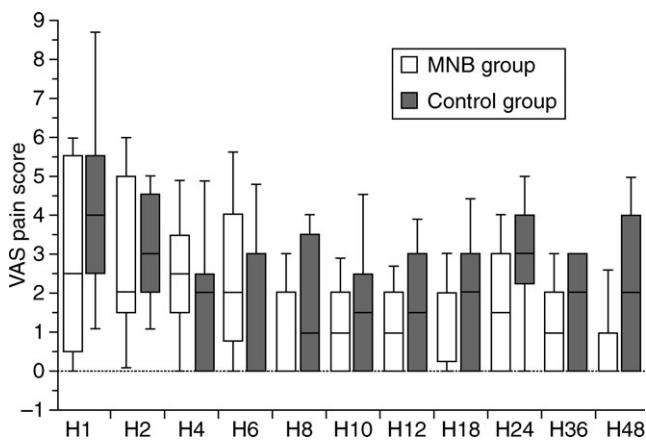


Fig 2 Pain reported using the VAS score. The box represents the 25th–75th percentiles, the dark line is the median, and the extended bars represent the 10th–90th percentiles. No significant difference was found between the two groups.

Discussion

In this randomized double-blind study, MNB performed at the foramen ovale before GA improved immediate postoperative analgesia after surgery for oropharyngeal carcinoma. In the MNB group, the mean cumulative consumption of morphine was reduced by 56 and 45% at 12 and 24 h after operation, respectively. Fewer patients experienced severe pain during the first postoperative day, and adequate analgesia (as defined as a mean VAS of ≤ 3) was observed throughout the study period in both groups except during the first 4 h after operation in the control group.

These results were obtained using the extra-oral lateral approach to the mandibular nerve that allows blocking of all the sensory branches of the mandibular nerve. For oropharyngeal surgery, this technique was preferred to intra-oral approaches because the latter, mainly used for lower molar extraction, do not consistently block the buccal nerve supplying the skin of the cheek over the buccinator muscle, the mucous membranes of the mouth, and part of the gums in the same area.^{6 15 16} The blood aspiration rate of 26.3% observed during the injection is comparable with the rates reported with conventional intra-oral blocking.^{16 17} The blood aspiration is related to the puncture of the maxillary artery or the pterygoid plexus of veins in the infra-temporal fossa.^{10 12} The effusion of blood is limited, because the fossa is filled by the temporalis muscle, and was not associated with any adverse sequelae in our study. Nevertheless, it is important to perform this block with caution and to aspirate for blood both before and during incremental injection of the anaesthetic solution. Paraesthesia is commonly elicited in the context of MNB.¹³ There is no consensus on the mean distance for which the needle must be inserted to reach the mandibular nerve.^{12 13} In our study, we used the distance between the site of puncture and the pterygoid plate as described previously.¹² This distance was recently found to be slightly longer than that between the site of puncture and the ovale foramen on dried skulls.¹⁸ Conversely, in a clinical study, the distance to the point where paraesthesia of mandibular nerve occurred was greater than that to the pterygoid plate.¹³ A large volume of anaesthetic solution, as described by Moore,¹⁹ was used to reduce the risk of block failure related to incorrect positioning of the needle.

The low level of pain experienced by the control group, using morphine PCA, and the large inter-individual variability in evaluation of pain explain, in part, why we did not demonstrate a statistically significant difference in pain score between the two groups. Furthermore, the rate of successful MNB was not evaluated to maintain patient blinding. Given the inflammatory nature of postoperative pain, the systematic administration of corticosteroids to all patients could also have contributed to the lack of difference in VAS pain scores. The extension of surgical resection to the area supplied by the maxillary nerve or the contralateral mandibular nerve in some patients is another

factor that might have played a part in reducing the benefit of MNB. Postoperative pain resulting from tracheostomy, lateral neck dissection for lymph node clearance, or pectoralis major flap reconstruction is also not prevented by MNB. Despite these limitations, morphine consumption was lower up to 24 h after operation in the MNB group. The fact that morphine consumption was reduced to the same extent in the MNB group whatever the type of surgery carried out has to be interpreted with caution because of the small number of patients in each group. However, these results suggest that the differences observed were not related to differences in surgical treatment between MNB and control groups. Achieving complete analgesia in patients undergoing resection and reconstructive surgery for intra-oral malignancy would require, depending on the extent of the resection, mandibular, maxillary, and cervical plexus nerve blocks performed unilaterally or bilaterally. To our knowledge, the efficacy of such combined blocks has never been evaluated after oropharyngeal surgery.

In a previous study, the efficacy of MNB performed with ropivacaine in dentistry was dose dependent.²⁰ Only 7.5 mg ml⁻¹ of ropivacaine produced adequate anaesthesia compared with 2 and 5 mg ml⁻¹ concentrations. With the highest concentration of ropivacaine, pinprick anaesthesia lasted for a median [interquartile range] of 5.9 [0.6] h and numbness of the lower lip lasted for 9.3 [5.4] h. The profile of morphine consumption in our study suggests that the efficacy of MNB performed with ropivacaine 10 mg ml⁻¹ was approximately 12 h, including the duration of surgery. Continuous MNB using an indwelling catheter might be useful in prolonging postoperative analgesia. Using the lateral extra-oral approach, several authors obtained long-term pain control without any side-effects in patients with fractured mandible,¹⁰ trigeminal neuralgia,⁹ or intractable cancer-related pain.¹¹ The feasibility and benefit of continuous MNB should be evaluated after oropharyngeal surgery.

Despite the high cumulative consumption of morphine, the incidence of adverse effects was low and comparable in the two groups of patients. The use of propofol, systematic administration of corticosteroids, and aspiration of gastric contents via a nasogastric tube in all patients might have contributed to reducing the overall incidence of postoperative nausea and vomiting.

In conclusion, our results demonstrate that MNB performed before GA for oropharyngeal cancer surgery improved postoperative analgesia, resulting in severe pain in fewer patients and reduced postoperative morphine consumption at 24 h.

References

- Mom T, Bazin JE, Commun F, *et al.* Assessment of postoperative pain after laryngeal surgery for cancer. *Arch Otolaryngol Head Neck Surg* 1998; **124**: 794–8
- Roussier M, Mahul P, Pascal J, *et al.* Patient-controlled cervical epidural fentanyl compared with patient-controlled i.v. fentanyl for pain after pharyngolaryngeal surgery. *Br J Anaesth* 2006; **96**: 492–6
- Nguyen A, Girard F, Boudreault D, *et al.* Scalp nerve blocks decrease the severity of pain after craniotomy. *Anesth Analg* 2001; **93**: 1272–6
- Mulroy MF, Larkin KL, Batra MS, Hodgson PS, Owens BD. Femoral nerve block with 0.25% or 0.5% bupivacaine improves postoperative analgesia following outpatient arthroscopic anterior cruciate ligament repair. *Reg Anesth Pain Med* 2001; **26**: 24–9
- Wang H, Bactor B, Verner J. The effect of single-injection femoral nerve block on rehabilitation and length of hospital stay after total knee replacement. *Reg Anesth Pain Med* 2002; **27**: 139–44
- Van Lancker P, Abeloos JV, De Clercq CA, Mommaerts MY. The effect of mandibular nerve block on opioid consumption, nausea and vomiting in bilateral osteotomies. *Acta Anaesthesiol Belg* 2003; **54**: 223–6
- Danielsson K, Evers H, Holmlund A, Kjellman O, Nordenram A, Persson NE. Long-acting local anaesthetics in oral surgery. Clinical evaluation of bupivacaine and etidocaine for mandibular nerve block. *Int J Oral Maxillofac Surg* 1986; **15**: 119–26
- Gordon SM, Dionne RA, Brahim J, Jabir F, Dubner R. Blockade of peripheral neuronal barrage reduces postoperative pain. *Pain* 1997; **70**: 209–15
- Umino M, Kohase H, Ideguchi S, Sakurai N. Long-term pain control in trigeminal neuralgia with local anesthetics using an indwelling catheter in the mandibular nerve. *Clin J Pain* 2002; **18**: 196–9
- Singh B, Bhardwaj V. Continuous mandibular nerve block for pain relief. A report of two cases. *Can J Anaesth* 2002; **49**: 951–3
- Kohase H, Umino M, Shibaji T, Suzuki N. Application of a mandibular nerve block using an indwelling catheter for intractable cancer pain. *Acta Anaesthesiol Scand* 2004; **48**: 382–3
- Stajcic Z, Todorovic L. Blocks of the foramen rotundum and the oval foramen: a reappraisal of extraoral maxillary and mandibular nerve injections. *Br J Oral Maxillofac Surg* 1997; **35**: 328–33
- Singh B, Srivastava SK, Dang R, Gombar KK, Gombar S. Anatomic considerations in relation to the mandibular nerve block. *Reg Anesth Pain Med* 1993; **18**: 181–3
- Dupont WD, Plummer WDJ. Power and sample size calculations: a review and computer program. *Control Clin Trials* 1990; **11**: 116–28
- Aker FD. Blocking the buccal nerve using two methods of inferior alveolar block injection. *Clin Anat* 2001; **14**: 111–9
- Donkor P, Wong J, Punnia-Moorthy A. An evaluation of the closed mouth mandibular block technique. *Int J Oral Maxillofac Surg* 1990; **19**: 216–9
- Martinez Gonzalez JM, Benito Pena B, Fernandez Caliz F, San Hipolito Marin L, Penarrocha Diago M. A comparative study of direct mandibular nerve block and the Akinosi technique. *Med Oral* 2003; **8**: 143–9
- Stajcic Z, Stojcev L, Mileusnic I, Djuric-Srejec M. Mandibular nerve block at the oval foramen using reliable landmarks: refinement of a previously described procedure. *Int J Oral Maxillofac Surg* 2002; **31**: 423–6
- Moore DC. Block of the mandibular nerve. In: Moore DC, ed. *Regional Block*, 4th Edn. Springfield: Charles C. Thomas, 1976; 93–111
- Ernberg M, Kopp S. Ropivacaine for dental anesthesia: a dose-finding study. *J Oral Maxillofac Surg* 2002; **60**: 1004–10