

PAIN

Analgesic efficacy of bilateral superficial cervical plexus block administered before thyroid surgery under general anaesthesia

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Background. The use of regional anaesthesia in thyroid surgery remains controversial. This double-blind, randomized controlled study was conducted to evaluate the analgesic efficacy of bilateral superficial cervical plexus block (BSCPB) performed under general anaesthesia in patients undergoing total thyroidectomy.

Methods. Eighty-seven consecutive consenting patients were randomized to receive a BSCPB with saline (Group P, $n=29$), ropivacaine 0.487% (Group R, $n=29$), or ropivacaine 0.487% plus clonidine $5 \mu\text{g ml}^{-1}$ (Group RC, $n=29$). Sufentanil was given during the intraoperative period for a 20% increase in arterial mean pressure or heart rate in a patient with a bispectral index between 40 and 60. All patients received 4 g of acetaminophen during the first 24 h after operation. The pain score was checked every 4 h and nefopam was given for pain score >4 on a numeric pain scale.

Results. During surgery, the median sufentanil requirements were significantly reduced in Group RC compared with Groups R and P (0.32 vs 0.47 and $0.62 \mu\text{g kg}^{-1}$; $P<0.0001$). After surgery, the number of patients requiring nefopam within 24 h of surgery was significantly lower in Groups R and RC than in Group P (16 and 19 vs 25; $P=0.03$). At post-anaesthetic care unit admission, median (range) pain scores were significantly lower in Groups R [3 (0–10)] and RC [3 (0–8)] than in Group P [5 (0–8), $P=0.03$]. No major complications of BSCPB occurred during study.

Conclusions. BSCPB with ropivacaine and clonidine improved intraoperative analgesia. BSCPB with ropivacaine or ropivacaine and clonidine was effective in reducing analgesic requirements after thyroid surgery.

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Pain after thyroid surgery is regarded as being of moderate intensity and short duration.¹ However, during the first 24 h after surgery, some patients require opioid and non-opioid analgesics. In a study by Gozal and colleagues,² the mean pain level estimated on a 100 mm visual analogue scale (VAS) was 69 mm and 90% of the patients required opiates. Another group reported that 70% of the patients had pain levels above 40 mm measured on a VAS, despite an analgesic regimen based on acetaminophen.³ In addition, thyroid surgery is reported to be associated with

a high risk of postoperative nausea and vomiting (PONV).³ Analgesics inducing nausea or vomiting, such as opioids or nefopam, should be avoided.⁴

Bilaterally superficial cervical plexus block (BSCPB) may reduce analgesic requirements. This technique consists of a bilateral injection of local anaesthetic behind the lateral border of the sternocleidomastoid muscle producing surface anaesthesia of the neck. A two- or three-point injection technique can be used. Unlike the two-point technique, the three-point technique (Fig. 1) allows blockade of

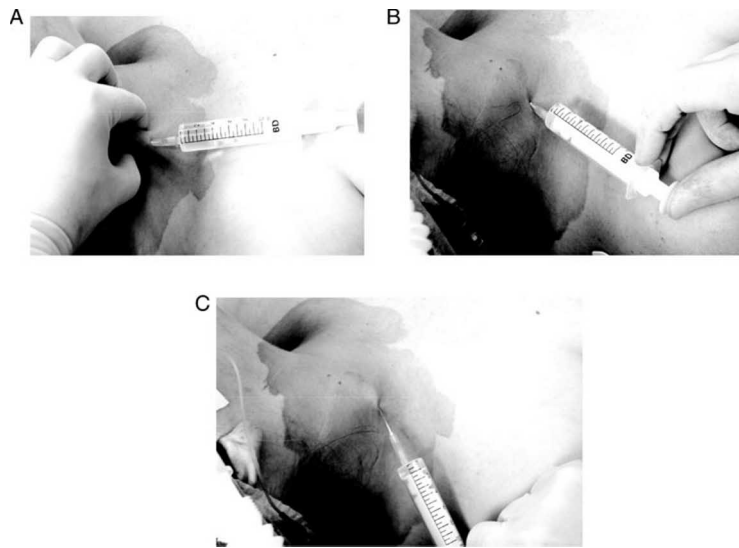


Fig 1 Cervical plexus block using a three-point injection technique. (A) An s.c. injection of 6 ml of the prepared mixture was performed in the cephalic direction along the posterior border of the clavicular head of the sternocleidomastoid muscle. (B) The needle was reoriented in the medial direction above the sternocleidomastoid muscle and 3 ml of the prepared mixture were injected. (C) The last s.c. injection aimed to block the supraclavicular nerve. This third injection is omitted in the two-point injection technique.

the transverse cervical branches of the plexus. (A full description of block technique is given in the Methods.) However, the effectiveness of this technique in decreasing the levels of pain after thyroidectomy is debated. Dieudonne and colleagues⁵ used a three-point injection and showed that BSCBP using 10 ml of bupivacaine 0.25% with 1:200 000 epinephrine decreased the intensity of postoperative pain and postoperative opioid requirement. In this study, cervical block was performed at the end of the surgery. Therefore, it did not decrease opioid consumption during surgery or the incidence of PONV thereafter. Moreover, due to the slow onset of bupivacaine (>20 min),⁶ there was an increased demand for analgesics in the post-anaesthetic care unit (PACU). Two recent studies using a two-point injection technique or wound infiltration did not find any analgesic effect of BSCPB.^{7 8} In those studies, regional analgesia was performed without any adjuvant such as epinephrine or clonidine. The addition of clonidine may improve the quality⁹ and increase the duration of analgesia.¹⁰ Danelli and colleagues⁹ reported that adding 50 µg of clonidine to 150 mg of ropivacaine for superficial cervical plexus block shortened the onset time and improved the quality of surgical anaesthesia in patients undergoing elective carotid endarterectomy. Moreover, the addition of clonidine 1 µg kg⁻¹ to ropivacaine 0.75% prolongs the duration of postoperative analgesia by 3 h.¹⁰

This double-blind, randomized controlled study in patients undergoing thyroid surgery was conducted to evaluate the effects of a three-point BSCPB, performed immediately after induction of general anaesthesia, with ropivacaine 0.487% with either clonidine or placebo, on nefopam requirements after surgery. The secondary

objectives were to compare intra-operative analgesic consumption and the incidence of postoperative side-effects in the study groups.

Methods

The study was approved by the ethics committee for Human Investigations of the University of Lille. Written informed consent was obtained from participating patients. Ninety ASA physical status I–II adult patients undergoing elective thyroid surgery under general anaesthesia were included. Patients were randomized by computer-generated tables into three groups to receive isotonic sodium chloride solution (Group P), 0.487% plain ropivacaine (Naropeine®, Astra-Zeneca, Söderjälje, Sweden) (Group R), or 0.487% ropivacaine plus clonidine (Catapressan®, Boehringer Ingelheim, Reims, France) 75 µg (Group RC). The concentration used was based on that proposed by Aunac and colleagues,¹¹ who used ropivacaine 0.5%. The mixture was prepared with 6.5 ml of ropivacaine 0.75% and 3 ml of saline in Group R and 6.5 ml of ropivacaine 0.75% with 2.5 ml of saline and 0.5 ml of clonidine, that is, 75 µg, in Group RC. The injection was given with unlabelled syringes prepared by a nurse not involved in the patients' care or in pain assessment. The specific treatment given was unknown to the patient, anaesthesiologist, surgeon, or nurses in charge of pain assessment.

The patients were excluded from the study if their pre-operative medication included opioid or non-opioid analgesics, corticosteroids, or non-steroidal anti-inflammatory drugs. Coagulation disorders, pregnancy, age less than 18 yr, patient refusal, and emergency re-operation within

the first 24 h also were exclusion criteria. Because of the limited sensory territory blocked by the BSCPB, patients with substernal goitres or requiring thyroidectomy with lymph node dissection were not included in the study.

Anaesthesia was standardized. Patients were premedicated with hydroxyzine (1.5 mg kg^{-1} orally) 2 h before surgery. General anaesthesia was induced using propofol ($2\text{--}3 \text{ mg kg}^{-1}$) and sufentanil ($0.3 \text{ } \mu\text{g kg}^{-1}$). Tracheal intubation was facilitated by the administration of atracurium 0.5 mg kg^{-1} . General anaesthesia was maintained with sevoflurane ($0.5\text{--}1.8\%$) in an oxygen–nitrous oxide mixture (60/40%). The sevoflurane was adjusted to maintain a bispectral index (BIS; AspectMedical Systems, Inc., Newton, MA, USA) between 40 and 60. Additional doses of sufentanil ($0.15 \text{ } \mu\text{g kg}^{-1}$) were administered for variations of systolic blood pressure (SBP) and heart rate (HR) of more than 20% when compared with the values measured before operation. All the patients were admitted to the PACU.

BSCPB was performed by an anaesthesiologist familiar with the technique, under general anaesthesia, before incision. Using a three-point injection technique, 10 ml of the prepared mixture were injected in each side using the same puncture orifice. A 23-Gauge, s.c., short bevelled needle (23 Gauge, DataBase Microlance™3, Dublin, Ireland) was inserted 2 cm above the clavicle along the posterior border of the clavicular head of the sternocleidomastoid muscle (Fig. 1A). After an aspiration test, an s.c. injection of 6 ml of the prepared mixture was performed in the cephalic direction. Then the needle was reoriented in the medial direction above the sternocleidomastoid muscle and 3 ml of the prepared mixture were injected (Fig. 1B). These two first injections allow anaesthesia of the great auricular and transverse cervical nerves. Finally, 1 ml of the mixture was injected s.c. at the point of puncture to block the supraclavicular nerves (Fig. 1C). The depth of mixture injection was not $>5 \text{ mm}$ in order to prevent the block of the phrenic or recurrent laryngeal nerve. Postoperative laryngoscopy was performed to evaluate laryngeal palsy before transfer to the PACU.

Intraoperatively, SBP and HR were recorded by a computer at induction, incision, end of resection, and extubation. The duration of surgery and sufentanil requirements were also recorded.

Postoperative pain was assessed by a numeric rating scale (NRS) ranging from 0 (no pain) to 10 (worst imaginable pain). All patients received 15 mg kg^{-1} i.v. acetaminophen every 6 h; the first dose was given 40 min before the end of surgery. Additionally, i.v. nefopam (Acupan®, Biocodex, Beauvais, France) (20 mg for 20 min with a maximum of 120 mg for 24 h) was given to patients with an NRS higher than 4. Pain level was recorded at PACU admission (H0) when the patient was able to communicate, then every 3 h for the first 12 h and every 6 h until the 24th hour (H3, H6, H9, H12, H18, and H24). Any episodes of bradycardia ($\text{HR} < 40 \text{ beats min}^{-1}$), hypotension

($\text{SBP} < 85 \text{ mm Hg}$), nausea, vomiting, and excessive sedation were recorded during the first 24 h after surgery.

The primary outcome was the nefopam requirement of the different groups during the first 24 h after total thyroidectomy. The secondary outcomes were intraoperative sufentanil requirements and haemodynamic differences between the groups. The quality of analgesia and all adverse events related to surgery and the regional anaesthetic technique were also recorded.

In a pilot study of 24 patients (12 without BSCBP and 12 after BSCBP with ropivacaine 0.487%), we observed lower nefopam requirements in patients with BSCBP (mean difference: 8 mg and standard deviation: 13.3 mg). A 50% reduction in the postoperative dose of nefopam in BSCBP groups was considered to be clinically significant. We calculated that 27 patients were required in each group to ensure a power of 0.90 with an α error of 0.05.

Continuous variables are reported as median (range). The differences between groups were examined with the Kruskal–Wallis test. *Post hoc* testing was performed using the Mann–Whitney test. Within-group comparisons were made using Friedman's test. Categorical variables are reported as proportions and were analysed using the χ^2 test or Fisher's exact test. A value of $P < 0.05$ was considered statistically significant. All the statistical tests were carried out using the Statview® software Version 5.0 (SAS Institute Inc., Cary, NC, USA).

Results

All 90 patients enrolled completed the study protocol, but three were excluded because of incomplete pain data. Patient characteristics were similar in the three groups except for gender, with fewer females in Group RC (Table 1).

SBP was significantly lower in Group RC compared with the other groups at the end of resection and at extubation (Table 2). The maximum reduction in SBF compared with induction was 28% for Group RC and 24% for Groups R and P. No significant difference in blood pressure was observed between Groups R and P. HR did not differ between the groups.

Intra- and postoperative analgesic requirements are summarized in Table 3. Sufentanil requirements were

Table 1 Patients' characteristics. Data are expressed as mean (range), mean (SD) or number (percentage)

	Group P (n=29)	Group R (n=29)	Group RC (n=29)
Age (yr)	47 (24–67)	48 (28–79)	48 (24–77)
Height (cm)	164.5 (7.0)	165.3 (8.7)	167.0 (8.2)
Weight (kg)	71.3 (12.2)	72.5 (14.5)	79.5 (20.0)
Duration of surgery (min)	182.2 (46.9)	183.8 (52.0)	207.0 (62.0)
Female (%)	28 (96.6)	24 (82.8)	20 (69.0)

Table 2 SBP in mm Hg (median, range) recorded at induction, incision, end of resection, and extubation. The column *P*-value gives the results of a comparison between the three groups by the Kruskal–Wallis test. *Indicates a statistically significant difference ($P<0.05$) between P vs R or RC. #Indicates a statistically significant difference ($P<0.05$) between R and RC by the Mann–Whitney *U*-test

	Group P	Group R	Group RC	<i>P</i> -value
Induction	159 (220–110)	150 (194–112)	158 (224–110)	0.42
Incision	116 (215–85)	116 (146–87)	113 (180–86)	0.79
End of resection	143 (170–101)	135 (180–110)	120 (182–82)*, #	0.005
Extubation	162 (220–118)	150 (209–120)	140 (190–104)*, #	0.001

significantly reduced in Group RC compared with Groups P and R ($P<0.005$). Nefopam requirements during the first 24 h after thyroidectomy were significantly reduced in Groups R and RC compared with Group P ($P=0.03$), but no difference was observed between R and RC. Because of the difference in the gender distribution between the groups, data for the female patients were analysed separately. (There were too few male patients to allow a valid analysis of this subgroup.) In this analysis, 66.7% (16/24) of female patients in Group R and 60% (12/20) of female patients in Group RC required nefopam in the postoperative period compared with 85.7% (24/28) in Group P ($P<0.05$). The proportion of patients requiring nefopam at different postoperative times is shown in Figure 2. At PACU admission, 79% of the patients in Group P required nefopam compared with 35% in Group R and 34% in Group RC. At H3, only 17% of the patients required nefopam in Group RC compared with 41% in Group R and 38% in Group P, respectively. Finally from H6 to the end of the study, no rebound in nefopam requirement was observed in Groups R and RC.

At PACU admission, pain scores were significantly lower in Groups R median (range) 3 (0–10) ($P=0.01$) and RC 3 (0–8) ($P=0.004$) than in Group P 5(0–8) (Fig. 3). Pain scores decreased in all three groups during the 24 h after surgery. At the end of the study, these were median (range) 1 (0–5) in Group P, 1 (0–4) in Group R, and 1 (0–4) in Group RC. Fourteen (48%) patients in the

placebo group had an NRS pain score of 6 during the first 24 h, compared with 7 (24%) patients in Group R and 5 (17%) patients in Group RC. The proportion of patients whose NRS was greater than 6 during the 24 h after surgery was significantly fewer in Groups R and RC than in Group P (Table 3).

Thirty-one patients (36%) developed PONV, eight patients in Group P, 14 patients in Group R, and nine patients in Group RC ($P=0.21$). PONV occurred in the PACU in 28 patients (90.3% of the patients who developed PONV). Immediately after surgery, direct laryngoscopy revealed a transient vocal cord paresis in four patients in Group P, in two patients in Group R, and in eight patients in Group RC ($P=0.09$). No other adverse event was noted in any group.

Discussion

In this study, we demonstrated that BSCPB, performed immediately after the induction of general anaesthesia in patients undergoing thyroid surgery using a three-point technique with ropivacaine 0.487%, with or without clonidine, significantly reduced postoperative analgesic requirement. The fact that the RC group had the lowest intraoperative sufentanil requirement suggests that the addition of clonidine to ropivacaine improves intraoperative analgesia.

Dieudonne and colleagues⁵ pointed out the value of the BSCPB after thyroidectomy. In their study, half of the patients in whom a BSCPB was performed did not require opiate analgesics during the first two postoperative hours and 34% did not require opiate analgesics during the first 24 h after surgery. Another study reported a reduction in intra- and postoperative analgesic requirement with bilateral superficial and deep cervical plexus block performed with 0.5% plain ropivacaine with or without clonidine.¹¹ The value of BSCPB in thyroid surgery is, however, debated. Herbland and colleagues did not find an analgesic effect of BSCPB with 0.75% ropivacaine administered before or

Table 3 Intra- and postoperative analgesic requirement during the first 24 h after surgery, pain scores in the PACU, and proportion of patients who had a pain score of 6 or more at any time during the first 24 h. Data are presented as median (range) or number of patients (%). The column *P*-value gives the results of a comparison between the three groups by the Kruskal–Wallis test. *Indicates a statistically significant difference ($P<0.05$) between P vs R or RC. #Indicates a statistically significant difference ($P<0.05$) between R and RC by the χ^2 test or Mann–Whitney *U*-test

	Group P (<i>n</i> =29)	Group R (<i>n</i> =29)	Group RC (<i>n</i> =29)	<i>P</i> -value
Intraoperative supplementary sufentanil ($\mu\text{g kg}^{-1}$)	0.616 (0.235–1.077)	0.473 (0.211–1.176)	0.321 (0.208–0.764)* #	0.0007
Pain scores in the PACU	5 (0–8)	3 (0–10)*	3 (0–8)*	0.03
Number of patients who had a pain score ≥ 6 at any time during the first 24 h after surgery	14 (48%)	7 (24%)*	5 (17%)*	0.02
Number of patients requiring nefopam at any time during the first 24 h after surgery	25 (86.2%)	19 (65.5%)*	16 (55.2%)*	0.03

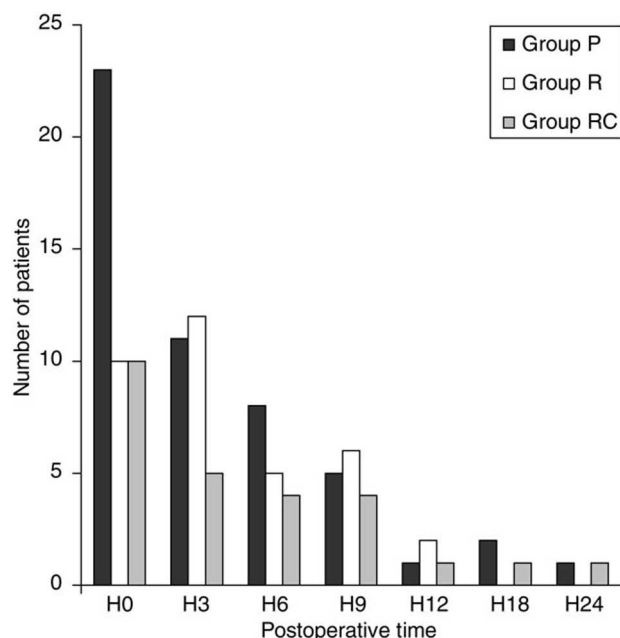


Fig 2 Nefopam requirements during the first 24 h after surgery. The graph shows the number of patients requiring a 20 mg dose of nefopam at each postoperative time point for each group. Patients in Group R had BSCPB performed with ropivacaine 0.487%, those in Group RC ropivacaine 0.487% plus clonidine 5 µg ml⁻¹, and those in Group P saline.

after surgery.⁷ However, Herbland and colleagues used a two-point injection for performing BSCPB, whereas we used a three-point technique. The two-injection technique blocks the main emerging branches of the superficial cervical plexus, whereas in the three-injection technique additional infiltration of the transverse cervical branches is achieved. Additional analgesia of this area may explain, at least in part, the difference observed in our study. Recently, BSCPB performed using a three-injection

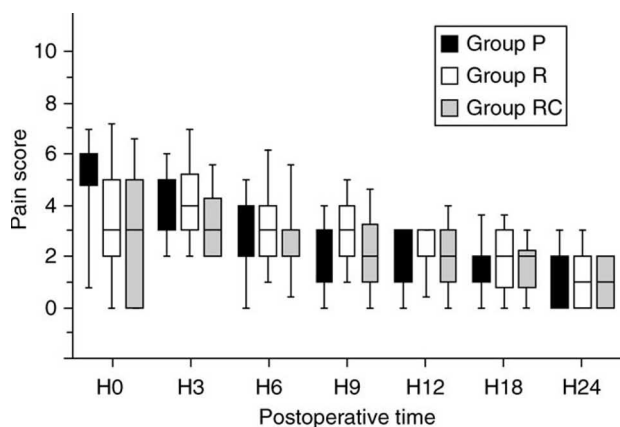


Fig 3 Box and whisker plot of pain scores during the first 24 h after surgery. Results are expressed as medians. The top and bottom of each box indicate the 75th and 25th percentiles, and the error bars the 10th and 90th percentiles. Patients in Group R had BSCPB performed with ropivacaine 0.487%, those in Group RC ropivacaine 0.487% plus clonidine 5 µg ml⁻¹, and those in Group P saline.

technique was reported to not reduce analgesic requirement after thyroid surgery. Forty-five patients were randomized to receive no regional analgesia (control) or BSCPB or local anaesthetic wound infiltration with either 30 or 20 ml of bupivacaine 0.25% performed after intubation. No significant reduction in postoperative opioid demand or pain scores was observed between groups, leading the authors to conclude that BSCPB or local anaesthetic wound infiltration with bupivacaine 0.25% did not decrease analgesic requirement after thyroid surgery.⁸ However, these authors performed their BSCPB with a low concentration local anaesthetic without any adjuvant such as epinephrine in Dieudonne's study⁵ or clonidine in our work. As a consequence, the block may have receded rapidly during the postoperative period, even though the time to first analgesic requirement was significantly longer in the BSCPB group compared with local anaesthetic wound infiltration or control groups. These studies suggest that the clinical benefit of BSCPB after thyroid surgery depends on the technique used.

In the present study, the greatest reduction in intraoperative analgesic requirement was seen in patients in whom BSCPB had been performed with a mixture of ropivacaine and clonidine. Clonidine is known to enhance pain relief after peripheral nerve block, probably via a central action due to systemic absorption and a direct action on local nerve fibres.¹² Because a significant reduction in SBF was only observed in the patients treated with ropivacaine and clonidine, systemic absorption may have been responsible for the enhanced block in our patients. Others have reported that the local analgesic effect of clonidine is affected by local inflammation.¹³ Consequently, the inflammatory reaction induced by the surgical stimulus may have increased its analgesic effect and may partly explain the reduction in intraoperative opioid requirement. The effect may also be mediated by a local action via drug interaction between ropivacaine and clonidine on local nerve fibres.¹²⁻¹⁴ Ropivacaine was chosen for its lesser cardiac toxicity compared with bupivacaine¹⁵ because for BSCPB significant volumes of local anaesthetic are injected near vascular structures. Aunac and colleagues¹¹ have demonstrated the safety of ropivacaine 0.5% for combined superficial and deep cervical plexus block in thyroid surgery.

The pain scores in the saline group confirm that after thyroidectomy, some patients experience severe pain (48% had a pain score >6) and that the duration of this pain is shorter than 24 h (the median score pain score at 24 h was 1). After thyroidectomy, the pain control should focus on the first postoperative hours. Acetaminophen alone is insufficient, as 82.6% of our patients in Group P had a score of pain ≥4 in the PACU and 86.2% of them required nefopam in the first 24 h. Regional anaesthesia is an appropriate component of multimodal analgesia in this setting. Furthermore, regional nerve blockade may also contribute to decreased mechanical hyperalgesia induced by inflammation.^{16 17}

Superficial cervical plexus block is probably sufficient for thyroid surgery. The serious complications that may be associated with deep cervical block, particularly phrenic nerve palsy, make it inappropriate to perform this block bilaterally. We observed no significant side-effects from superficial cervical plexus blockade. In particular, BSCPb was not associated with an increased incidence of recurrent nerve paralysis by diffusion of the local anaesthetic. Compared with bilateral deep cervical plexus block, BSCPb has the advantage of being devoid of serious complications as long as injection of local anaesthetic remains s.c.

Thyroid surgery is associated with a high incidence of PONV.³ In our study, 35.6% of the patients suffered PONV. No difference in incidence was observed between the three groups. The reduced intraoperative opioid consumption in patients blocked with ropivacaine plus clonidine was not sufficient to decrease the incidence of PONV. A similar result was reported in a study of mandibular osteotomies in which the reduced intraoperative opioid requirement induced by mandibular nerve block was not associated with a decrease in PONV.¹⁸ Several factors may have influenced the high incidence of PONV in our study, including volatile anaesthetic and nitrous oxide anaesthesia, absence of prophylactic antiemetics, the high number of female patients, and the use of nefopam.¹⁹

In conclusion, BSCPb is an effective technique to reduce analgesic requirements during and after thyroid surgery. The use of ropivacaine and clonidine improves intraoperative analgesia. Our data suggest that it is possible to manage pain after thyroid surgery with regional anaesthesia and acetaminophen.

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