

Analgesic efficacy of bilateral superficial cervical plexus block for thyroid surgery: meta-analysis and systematic review

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Abstract

Background: Thyroid surgery is moderately painful, but is increasingly being considered as a day-case procedure. Bilateral superficial cervical plexus block (BSCPB) provides an adjuvant technique to facilitate this approach, but there is great evidential heterogeneity in randomised controlled trials (RCTs) about its use.

Methods: A systematic search, critical appraisal, and analysis of RCTs was performed. Trials investigating preoperative or postoperative BSCPB compared with control in patients undergoing thyroid surgery via neck incision were included. Odds ratio (OR) and 95% confidence interval (95% CI) were calculated for dichotomous data, whilst continuous data were analysed using standard mean difference. Primary outcome was rescue analgesic requirement in the first 24 postoperative hours. Secondary outcomes were visual analogue scale (VAS) scores at 0, 4, and 24 h, time until first analgesic request, intra-operative analgesic requirements, length of hospital stay, and incidence of postoperative nausea and vomiting (PONV).

Results: Fourteen RCTs published between 2001 and 2016 including 1154 patients were included. The overall effect of BSCPB compared with control showed a reduction in analgesic requirement (OR 0.30; 95% CI 0.18, 0.51; $P < 0.00001$). There was improvement in VAS scores ($P < 0.002$) and time to first analgesic requirement in the BSCPB group ($P < 0.00001$). Length of hospital stay was reduced by 6 h by use of BSCPB. There was no significant change in the incidence of PONV with its use (OR 0.82; 95% CI 0.49–1.37; $P = 0.44$).

Conclusions: BSCPB offers analgesic efficacy in the early postoperative period for up to 24 h after thyroid surgery, with reduced length of hospital stay, but without any beneficial effect on PONV.

Keywords: bilateral cervical plexus block; cervical plexus; nerve block; postoperative pain; thyroidectomy

Thyroid surgery is a common short-stay procedure associated with mild to moderate postoperative pain of short duration.¹ It has been reported that up to 90% of patients require morphine during the first postoperative day.² The concept of pre-emptive analgesia is hypothesized to include

pre-incision administration of local anaesthetics to prevent central sensitization and therefore improve postoperative pain management.³ It has been demonstrated that the efficacy of pre-emptive analgesia varies with surgical site.⁴ Bilateral superficial cervical plexus block (BSCPB) has been utilized for

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Editor's key points

- The authors systematically reviewed the literature relating to the use of bilateral superficial cervical plexus block in providing analgesia after thyroid surgery.
- Meta-analysis revealed that analgesic requirements and length of hospital stay were reduced in the 14 studies (1154 patients) examined, while postoperative vomiting appeared not to be.

postoperative pain management of neck surgeries because of its ability to block the emerging branches of the superficial cervical plexus (lesser occipital, greater auricular, transverse cervical, and supraclavicular nerves).

BSCPB is a procedure with a low serious complication rate.^{5–7} The risks of phrenic nerve palsy and total spinal anaesthesia from injection into a dural cuff are restricted to blockade of the deep cervical plexus only; diffusion of local anaesthetic is not sufficient to account for these phenomena with a superficial technique.

There have been several randomised controlled trials (RCTs) investigating the analgesic efficacy of BSCPB for thyroid surgery, with conflicting results. Hence, the use of a regional technique to manage acute postoperative pain has remained controversial for this type of surgery. The aim of this meta-analysis is to further investigate the effect of BSCPB on postoperative pain after thyroid surgery.

Methods

The meta-analysis component of this systematic review was performed according to the criteria of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.⁸

Literature search

The systematic search was conducted in the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE (1966 to present), EMBASE (1980–2016), Google Scholar, and Scirus according to the current recommendations of the Cochrane Collaboration. The search strategy consisted of a combination of the following terms: 'bilateral cervical plexus block', 'cervical plexus'; 'nerve block'; 'postoperative pain'; and 'thyroidectomy'. The search was performed without language restrictions. Retrieved article lists were checked for relevant publications. In addition, we searched for and reviewed published abstracts from relevant anaesthetic meetings including the American Society of Regional Anesthesia and Pain Medicine (ASRA 2002–2016), the European Society of Regional Anaesthesia (ESRA 2006–2016), American Society of Anesthesiologists (ASA 2000–2016), and the European Society of Anaesthesiology (ESA 2008–2016). Searches were last performed on October 28, 2016.

Eligibility criteria

All RCTs investigating the analgesic efficacy of preoperative or postoperative BSCPB block using local anaesthetic with or without additives (clonidine, epinephrine), compared with a control group using saline/no block, in patients undergoing thyroid surgery via neck incision were included in this review. Trials comparing BSCPB with deep cervical plexus block were excluded.

Selection of included studies

Four authors (D.M., A.B., R.K., N.S.) scanned the article titles and abstracts retrieved by the initial search to exclude obvious irrelevant studies. These authors independently collected data using a standardized data sheet. This included title, author, study groups used, type of block and local anaesthetic used, types of surgery, premedication, timing of block, intra-operative and postoperative analgesic use, incidence of postoperative nausea and vomiting (PONV), and length of hospital stay. Authors were contacted by telephone or email to obtain or clarify data when necessary.

Critical appraisal

The Jadad score (1–5) provides an independently validated method of describing trial quality and was used to assess the included RCTs.⁹ Three of the authors (D.M., R.K., N.S.) scored each trial independently using the five-point validated quality index. These three authors reviewed the articles and assigned a final score by consensus when the initial scores differed. Authors A.B. and D.M. then repeated the risk of bias assessment using the internal processes within the RevMan software package (Review Manager (RevMan). Version 5.3. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014). This is a risk-of-bias tool that assesses to the QUADAS-2 standard and produces the risk of bias summary table that can be seen in Figure 1.

Study outcomes

All outcomes were described *a priori*, according to the principles of the PRISMA statement.⁸ The primary outcome variable for the meta-analysis was incidence of postoperative rescue analgesic requirement in the first 24 h after operation as described by the authors, with prospective subgroup analysis of preoperative vs postoperative blockade, two-point vs three-point injection technique, and saline vs no block administered. The BSCPB was administered either before operation; just after induction of anaesthesia and before skin incision, or immediately after the operation. The selection of studies was dependent on how authors described the timing of the administration of the block.

Two-point vs three-point injection techniques

Three-point injection as described by the authors blocked the lesser occipital, greater auricular, transverse cervical, and supraclavicular nerves compared with a two-point technique that excluded blocking the supraclavicular nerves. Selection of studies based on a three-point or two-point injection technique was dependent on how the authors described the procedure. The three-point injection trials describe a well-established landmark technique where local anaesthetic is subcutaneously infiltrated cranially and caudally along the posterior border of the sternocleidomastoid muscle, supplemented with an s.c. injection in the antero-posterior direction in order to anaesthetize the transverse cervical nerve.^{10–16} The two-point injection trials describe heterogenous techniques.^{17–19} Shih and colleagues¹⁷ describe a horizontal injection and a caudal injection, Herbland and colleagues¹⁸ describe a traditional cranial and caudal injection strategy, and Kesisoglou and colleagues¹⁹ describe a cranial and medial pattern.

The secondary outcomes were visual analogue scale (VAS) scores at 0, 4, and 24 h post-procedure, time interval until first

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)
Andrieu and colleagues 2007 (ropivacaine)					
Andrieu and colleagues 2007 (ropivacaine and clonidine)	+	+	+	+	+
Cai 2012	+	+	+	+	+
Dieudonne and colleagues 2001	+	+	+	+	+
Eti and colleagues 2006	+	?	+	+	+
Gurkan 2015	+	+	+	+	+
Herbland and colleagues 2006 (postoperative)					
Herbland and colleagues 2006 (preoperative)	+	+	+	+	+
Karthikeyan 2012 (bupivacaine and clonidine)					
Karthikeyan and colleagues 2012 (bupivacaine)	+	+	+	+	+
Kesisoglou and colleagues 2009	+	?	?	+	+
Moussa 2006	+	?	+	+	+
Negmi and colleagues 2005	?	+	+	?	?
Sardar 2013	?	?	+	?	+
Shih and colleagues 2010 (bupivacaine)					
Shih and colleagues 2010 (levobupivacaine)	+	+	+	+	+
Steffen and colleagues 2010 (postoperative)	+	+	+	+	+
Steffen and colleagues 2010 (preoperative)					
Suh and colleagues 2009	+	?	+	+	+

Fig 1. Risk of bias summary table. Note that missing data represents data that was split between two treatment arms for analysis. Each trial has been assessed once.

analgesic request, intraoperative analgesic requirements, length of hospital stay, and incidence of PONV. It was assumed that all patients who experienced vomiting would be nauseated as well and were considered as such for analysis of PONV. We assumed the analgesic requirement in Herbland and colleagues¹⁸ at 36 h to be comparable with 24 h. We considered T0 (postoperative) as the time when patients were admitted to post anaesthesia care unit/recovery and that the VAS score at 1 h after surgery to be equivalent to T0 for analysis purposes.²⁰

Statistical methods

The primary and secondary outcome data were inputted to Review Manager (RevMan; Version 5.3. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014) for statistical analysis. The odds ratio (OR) with the corresponding 95% confidence interval (95% CI) was calculated for dichotomous data. A statistically significant result occurred when the 95% CI did not include 1. A pre-specified subgroup analysis was performed to investigate the difference in

analgesic effect between preoperative and postoperative BSCPB. Continuous data were analysed using standard mean difference where a random-effect model was used. For all tests, statistical significance was defined as $P < 0.05$. Statistical heterogeneity was assessed using the I^2 test.

Three studies compared one control group against two different experimental groups. To avoid 'unit of analysis error' the control groups in these studies were divided equally for comparison with the experimental group.^{10,17,18} Information was extracted from the three studies which provided VAS score data in graphical format.^{12,16,17}

In studies where the results were reported as median and range,^{10,16,18} we considered the mean equivalent to the median and used the statistical formula $\text{range}/4$ to estimate the standard deviation (SD) from the range mentioned in these RCTs.²¹ For studies that quoted inter-quartile range (IQR) the SD was calculated using $\text{IQR}/1.35$. When standard error of the mean (SEM) was used, SD was calculated using $n^{1/2} \times \text{SEM}$. In addition, calculations were made to estimate a number needed to treat (NNT) for the primary outcome data.

For the primary outcome, the risk of bias in the studies was investigated by analysing the funnel plot. Harbord and colleagues²² regression test was performed to determine the significance of any publication bias. Sensitivity analysis was performed by restricting the analysis of the primary outcome excluding the outliers. After statistical analysis of the results, meta-regression was performed to investigate whether sample size, concentration, and type, dose or volume of local anaesthetic were responsible for heterogeneity. Subgroup analysis was performed regarding preoperative and postoperative BSCPB for the primary outcome, two-point vs three-point injection technique, and saline vs no block administered. When analysing data for 'intraoperative analgesic use' a conversion in the ratio of 1 μg :0.1 mg was used to convert fentanyl dose to morphine dose, and a conversion ratio of 1 μg :0.5 mg used to convert sufentanil dose to morphine dose.

Results

Description of included and excluded studies

Database searches yielded 48 relevant articles. After screening the title and abstract, 30 studies were identified as potentially relevant to meet the inclusion criteria. The full-text publications of these studies were examined in more detail. The data of 14 RCTs were included in the meta-analysis (Table 1).^{10–20,23–25} A total of 1154 participants with BSCPB were included in the study. All patients, except in three RCTs, received BSCPB under general anaesthesia.^{14,16,20} Study selection is described in Figure 2.

All included studies except Steffen and colleagues¹⁵ described standardized induction regimes. Eti and colleagues²³ induced anaesthesia with thiopental, the remainder with propofol (either as an infusion or a bolus). One trial did not describe the mode of induction of anaesthesia.¹⁵ Opioids were used as part of induction in the remainder of the studies.^{10–14,16–19,23–25} Anaesthesia was maintained by inhalation agents in nine studies,^{10–12,14,17,19,23–25} one study used total i.v. anaesthesia (TIVA) with propofol,¹⁸ and four studies used TIVA with propofol and remifentanyl.^{2,5,16,24} One study described no intraoperative analgesic use whatsoever.²³ Study characteristics are presented in Table 1.

Critical appraisal of study quality

All trials were RCTs. Study quality (Jadad score) was ≥ 3 in 11 studies,^{10–13,15–17,19,20,24,25} and ≤ 2 in the remaining three.^{14,18,23} Patients were blinded to the block except in the five studies where the control was no block, without a sham injection.^{18,20,23–25} Blinding to the group allocation of the tested intervention was performed in all studies. Intention to treat analysis was described in six of the included trials.^{10–12,15,17,20}

Primary outcome data

The primary outcome was incidence of use of postoperative rescue analgesia during the first 24 h. Eleven trials including 1035 patients were eligible for assessing this outcome.^{10–19,24} The trials included had a variety of definitions for the term 'rescue analgesia'. Five trials defined it as requiring a dose of morphine within the first 24 h,^{12–14,18,24} two as requiring paracetamol,^{10,15} one as requiring meperidine,¹⁶ and three that described 'rescue analgesia' but did not specify a drug.^{11,17,19} The number of patients requiring postoperative rescue analgesia was significantly lower in the BSCPB group compared with the control group during the first 24 h (OR: 0.30; 95% CI: 0.18, 0.51; $P < 0.00001$). A subgroup analysis of analgesic requirements between preoperative and postoperative BSCPB was performed. There were nine trials including 713 patients in the preoperative BSCPB group where the need for rescue analgesia was significantly less ($P < 0.00001$) compared with the four trials including 322 patients in the postoperative group ($P = 0.16$). Further subgroup analyses of the primary outcome demonstrated that there was a statistically significant difference between two-point ($P = 0.11$) and three-point injection techniques ($P = 0.002$) as there was between saline ($P < 0.00001$) vs no block ($P = 0.31$) with respect to rescue analgesia requirements. These data are summarized in Figure 3A–D.

Secondary outcomes

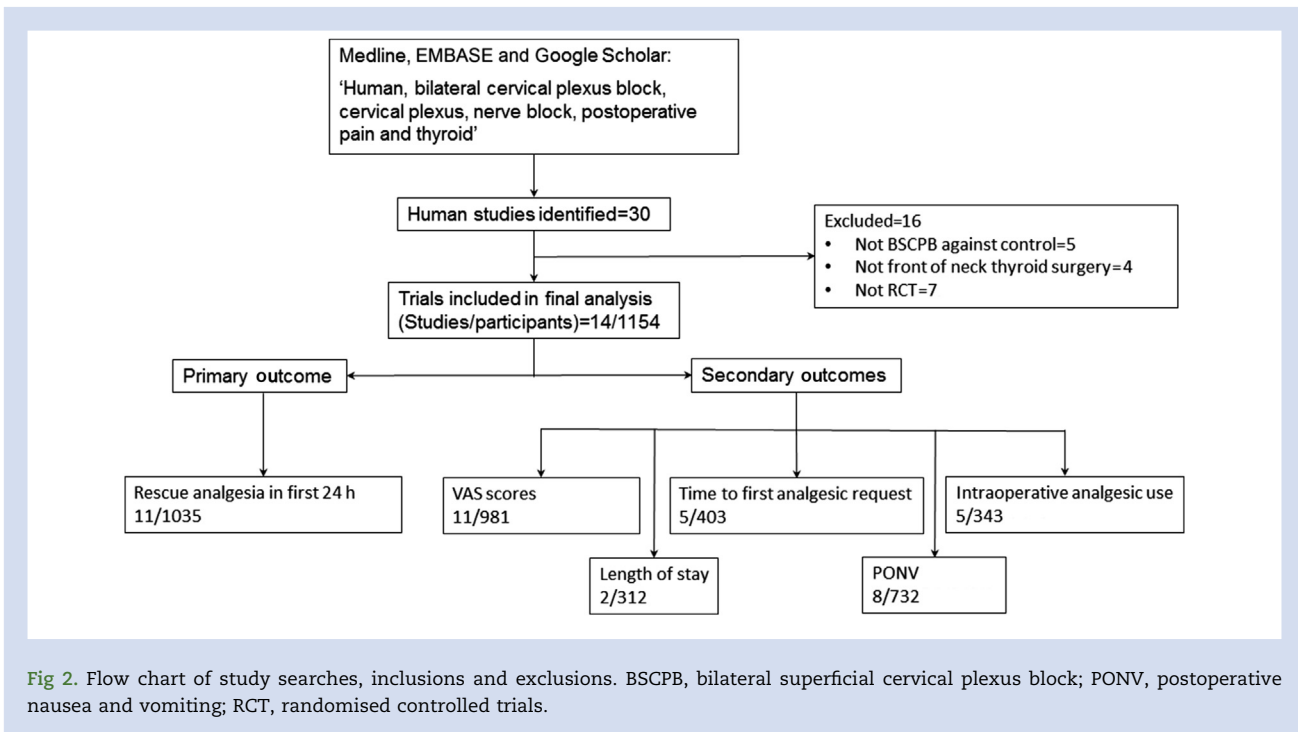
All secondary outcome data are summarized in Table 2. VAS scores at 0, 4, and 24 h were examined in 11 trials, including 981 patients.^{10–12,14,16–19,20,23,25} VAS scores at T0 were significantly lower in the BSCPB group ($P = 0.002$), demonstrating a mean reduction in absolute pain score from 4.74 to 3.55 with the addition of regional blockade. At 4 and 24 h post procedure, the results were also statistically significant ($P = 0.03$ and 0.01 , respectively). The mean time to first analgesic request was lengthened from 38.3 to 143 min with the addition of BSCPB based on data including 403 patients from five trials.^{13,17,18,23,25} These trials did not make clear how patients who did not require rescue analgesia were included into their analyses, if any such patients existed.

Intraoperative analgesic use was also subgroup analysed with regards to preoperative and postoperative block administration. In the preoperative block group, 182 patients were analysed from three trials.^{10,13,18} No statistically significant difference ($P = 0.05$) was observed in the total equivalent dose of morphine that was administered in this group.^{10,13,18} The postoperative block cohort analysed 161 patients from two trials and did not reach statistical significance either ($P = 0.44$).^{12,18} However, the overall treatment effect analysis demonstrated a statistically significant difference in morphine equivalent administration between control and BSCB patients ($P = 0.04$).

Table 1 Characteristics of included trials

Reference	Method of randomization	Groups	Timing of block	Block details	Control group	Types of surgery included	Premedication	Intraoperative analgesia	Postoperative analgesia	Jadad score
Andrieu and colleagues ¹⁰	Computer generated tables	BSCPB n=29 Control n=29 BSCPB+clonidine n=29	Pre-incision	Three-point, 9.5 ml each side	0.9% Saline	Total thyroidectomy	Hydroxyzine	Sufentanil	I.V. paracetamol (6 h); i.v. nefopam (pain score >4)	5
Dieudonne and colleagues ¹²	Random number sequence	BSCPB n=47 Control n=40	Post-incision	Three-point, 10 ml each side	0.9% Saline	Mixed thyroid surgery	Midazolam	Sufentanil; Propacetamol	I.V. paracetamol (6 h); i.v./s.c. morphine (pain score ≥4)	5
Eti and colleagues ²³	Randomly numbered sealed envelopes	BSCPB n=15 Control n=15	Pre-incision	Three-point, 15 ml each side	No block	Unspecified thyroid surgery	Midazolam	Nil	I.V. meperidine PCA	2
Herbland and colleagues ¹⁸	Randomly numbered sealed envelopes	Pre BSCPB n=37 Post BSCPB n=37 Control n=37	Pre- and post-incision	Two-point, 10 ml each side	No block	Total thyroidectomy	Hydroxyzine	Sufentanil; i.v. paracetamol	I.V./s.c. morphine	1
Karthikeyan and colleagues ¹³	Block randomization and serially numbered envelopes	BSCPB n=20 BSCPB+clonidine n=20 Control n=20	Pre-incision	Three-point, 15 ml each side	0.9% Saline	Mixed thyroid surgery	Diazepam	Fentanyl	I.V./PCA morphine	4
Kesisoglou and colleagues ¹⁹	Computer generated tables	BSCPB n=50 Control n=50	Post-incision	Two-point, 10 ml each side	0.9% Saline	Total thyroidectomy	Hydroxyzine	Sufentanil	I.V. parecoxib; dextropropoxyphene hydrochloride (PRN)	3
Moussa ²⁴	Not described	BSCPB n=12 Control n=12	Pre-incision	Single-point, 10 ml each side	No block	Mixed thyroid surgery	Midazolam	Remifentanyl infusion	I.V. paracetamol; i.v./s.c. Morphine	4
Negmi and colleagues ¹⁴	Not described	BSCPB n=25 Control n=25	Pre-induction	Three-point, 10 ml each side	0.9% Saline	Unspecified thyroid surgery	Midazolam	Fentanyl; diclofenac	Morphine	1
Rahman and colleagues ²⁵	Sealed envelopes	BSCPB (B) n=30 Control n=30	Pre-incision	Two-point, 10 ml each side	No block	Unspecified thyroid surgery	Nil	Nil	I.M. meperidine (PRN)	4
Shih and colleagues ¹⁷	Randomly numbered sealed envelopes	BSCPB (B) n=52 BSCPB (L) n=54 Control n=56	Pre-incision	Two-point, 12 ml each side	0.9% Saline	Mixed thyroid surgery	Nil	Fentanyl	Ketorolac (PRN)	5
Steffen and colleagues ¹⁵	Randomly numbered sealed envelopes	BSCPB pre n=41 BSCPB post n=41 Control pre n=38 Control post n=39	Pre- and post-incision	Three-point, 10 ml each side	Unspecified placebo solution	Mixed thyroid surgery	Nil	Nil	Oral paracetamol (PRN); Oral metamizole (PRN)	5
Suh and colleagues ¹⁶	Random number sequence	BSCPB n=30 Control n=30	Pre-incision	Three-point, 9 ml each side	Unspecified control solution	Thyroid lobectomy	Zolpidem tartrate	Nil	Diclofenac or pethidine (PRN)	3
Cai and colleagues ¹¹	Random numbers sealed envelopes	BSCPB n=67 Control n=68	Pre-Incision, post- induction	Three-point, 10 ml each side	0.9% Saline	Thyroidectomy	Nil	Flurbiprofen 1 mg kg ⁻¹	Fentanyl 50 µg	5
Gürkan and colleagues ²⁰	Sequentially numbered opaque sealed envelope	BSCPB n=25 Control n=25	Pre-induction	Single-point, 10 ml each side	Unspecified	Mixed thyroid surgery	Midazolam	Lornoxicam 8 mg, Paracetamol 1 g	Morphine PCA	4

BSCPB, bilateral superficial cervical plexus block; PCA, patient controlled analgesia; PRN, *pro re nata*.



Duration of hospital stay was statistically significantly shortened by the use of BSCPB, although only two trials (321 patients) were suitable for analysis, with the mean reduction in stay being approximately 6 h between the groups having received BSCPB (2.07 days) compared with control (2.35 days).^{15,17} The incidence of PONV did not decrease with the use of BSCPB (OR 0.82; 95% CI 0.49, 1.37; $P=0.44$).

Analysis for bias and internal consistency

Meta-regression of the data for sample size, Jadad score, local anaesthetic drug choice, local anaesthetic concentration, local anaesthetic volume and dose, method of injection, and use of adjuvants demonstrated no significant evidence of influence on results (these data are summarized in Table 1). The results of the Jadad scoring process and the compilation of the risk of bias summary table (Fig. 1) demonstrate no appreciable difference between the two scoring methods. There are methodological flaws in particular with Negmi and colleagues,¹⁴ but consensus was reached that it should be included. Subsequent sensitivity analysis revealed that its inclusion does not significantly alter the results of the outcome analyses. A funnel plot of the results showed no obvious asymmetry (Fig. 4) and no publication bias, which has been confirmed with the application of Begg and Mazumdar's²⁶ and Egger and colleagues tests.²⁷ We found that 'BSCPB vs no block' was better than 'BSCPB vs saline' thereby supporting the assertion that the use of 0.9% saline as a control has a possible role in inducing pain, although at present there are no randomized control trials investigating this effect.^{7,12}

Discussion

Primary outcome data

The primary outcome data from this meta-analysis demonstrate reduction in the requirement for rescue analgesia in the

first 24 h in patients who have received BSCPB for thyroid surgery. Subgroup analysis demonstrates that there may be a benefit if the block is undertaken before operation, and postoperative blockade appears to have no benefit over control. These findings have implications for the delivery of anaesthesia for thyroid surgery, as the use of postoperative BSCPB may result in more postoperative pain when compared with a preoperative block. Performing BSCPB before operation reduces the postoperative analgesic requirement compared with block performed after operation ($P<0.00001$). This is a phenomenon that is widely reported but has not yet been proved beyond doubt, and is not consistently described in thyroid surgery.²⁸ Of relevance is that whilst seven trials (713 patients) were included in the preoperative blockade cohort,^{10,11,13,14,16,17,24} there were only four trials (322 patients) reporting BSCPB performed in the postoperative period,^{12,15,18,19} one of which directly compared preoperative and postoperative blockade.¹⁵ Using the pooled risk difference of -0.23 ascertained from the primary outcome data, the calculated NNT was 4.4 for the overall use of BSCPB. However, in the subgroup analysis, for the BSCPB group that received the intervention before operation, the calculated NNT was 3.7 compared with 10 for the intervention group that received the BSCPB after operation. The limitation being that although there were no subgroup differences observed ($P=0.05$) there were differences in the numbers ($n/N=9/713$) in the preoperative compared with postoperative ($n/N=4/322$) BSCPB groups, which may have accounted for the observed differences in the calculated NNT (where n =number of trials; N =number of patients).

Outcomes with different injection techniques

Further subgroup analysis demonstrated that there was benefit to a three-point injection technique compared with a two-point technique (OR 0.35; 95% CI 0.19, 0.62; $P<0.0004$). However, compared with the three-point technique ($n=7/622$),

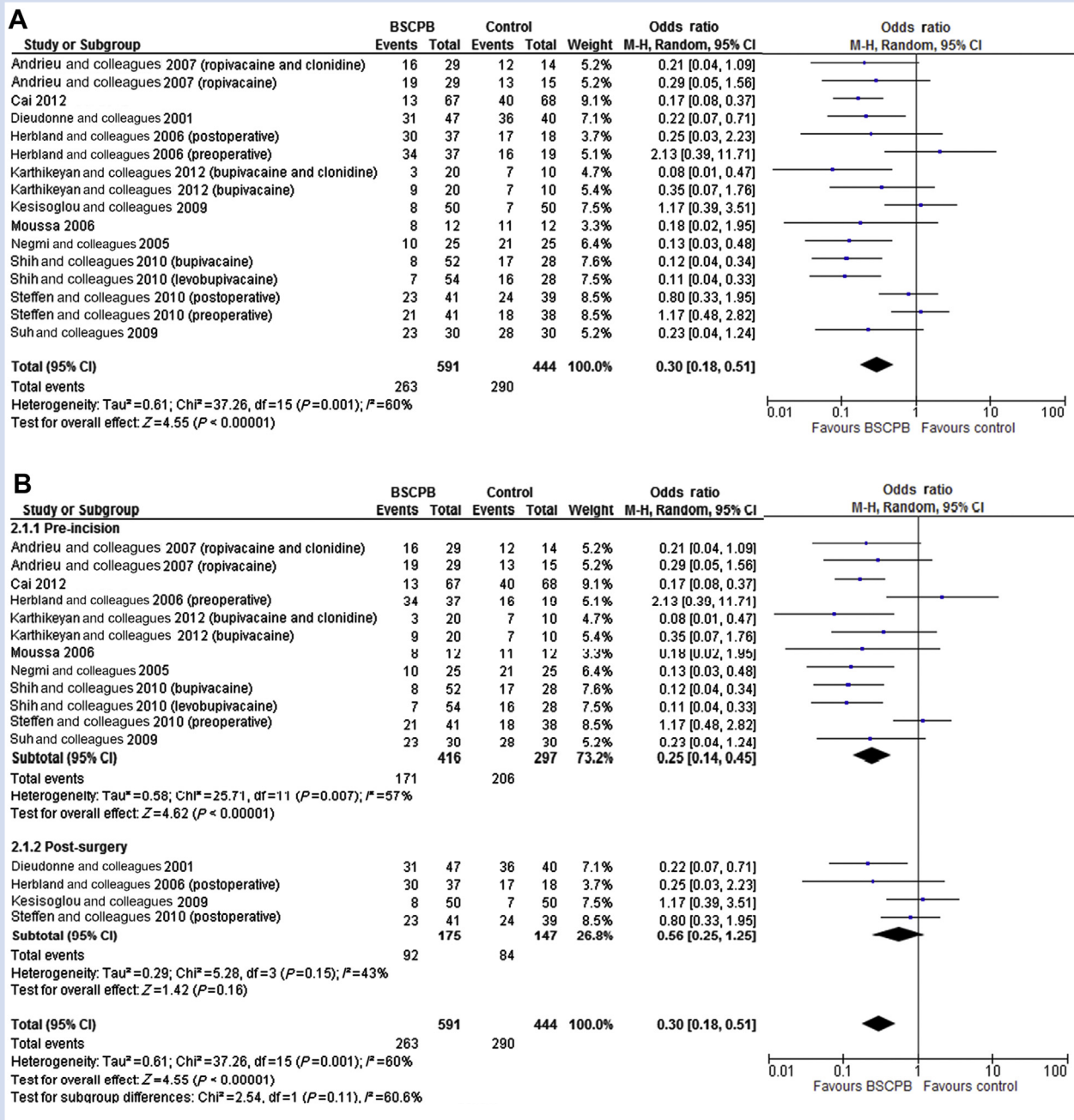


Fig 3. A) Forest plot of comparison for primary outcome data: incidence of use of postoperative rescue analgesia during the first 24 hours after surgery, with and without the use of BSCPB. B) Forest plot of comparison for primary outcome data: incidence of use of postoperative rescue analgesia during the first 24 h after surgery, subgrouped to delineate treatment effects with preoperative BSCPB or postoperative BSCPB. C) Forest plot of comparison for primary outcome data: incidence of use of rescue analgesia during the first 24 h after surgery, subgrouped to delineate treatment effects with a two-point injection technique, and a three-point technique. D) Forest plot of comparison for primary outcome data: incidence of use of postoperative rescue analgesia during the first 24 h after surgery, subgrouped to delineate treatment effect in trials using a saline sham block for control, and those using no block for control. BSCPB, Bilateral superficial cervical plexus block; CI, confidence interval.

the number of trials/patients was less for the two-point technique ($n=3/373$) and whether that influenced the overall outcome is a matter of conjecture. Whilst there was no subgroup heterogeneity observed statistically ($I^2=0$), it should be noted that the two-point trials each had a different approach

to blockade of the plexus.^{17–19} Anatomically, it is possible that each of the described two-point injection techniques will have ‘missed’ part of the plexus, and the significant improvement in efficacy when using a three-point technique may suggest that complete plexus blockade is required for this type of

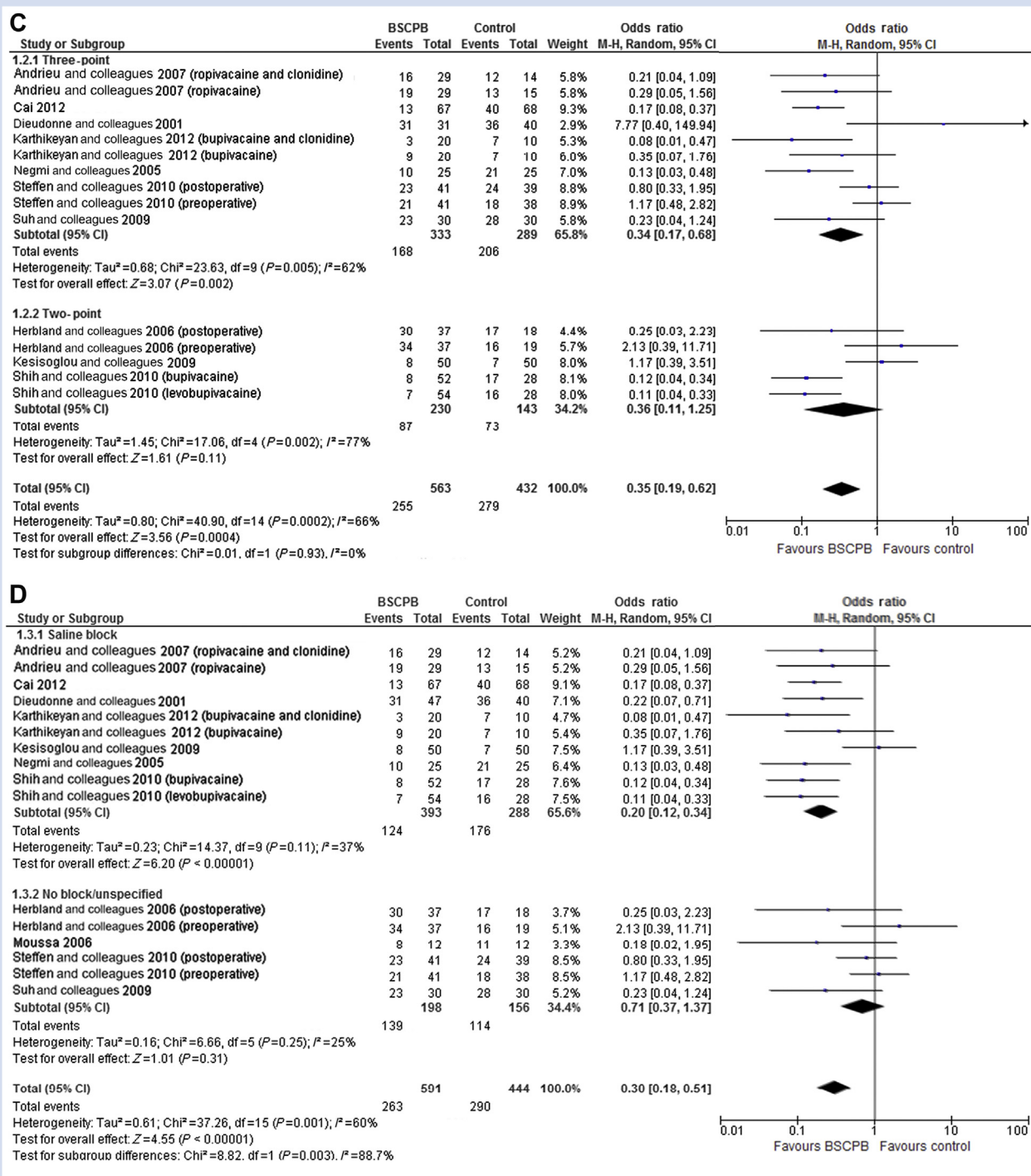


Fig 3. (continued).

surgery. Excluding outliers, the overall result or the direction did not change. For a three-point technique, the calculated NNT was 4.8 compared with NNT=5.5 for the two-point technique. Hence, more robustly conducted research is needed in this regard to conclude convincingly on the benefit/failure of the three- vs two-point technique, and to clarify if there is a suitable two-point injection technique that can produce acceptable plexus blockade.

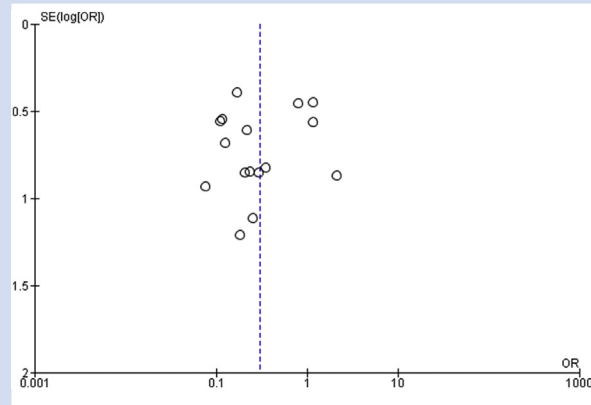
The saline control

Comparing BSCPB vs saline control techniques showed significantly superior pain relief (OR 0.20; 95% CI 0.12, 0.34; $P<0.00001$) in contrast to BSCPB vs no block (OR 0.71; 95% CI 0.37, 1.37; $P=0.31$). This probably highlights the concerns on the advantages and limitations of saline as a placebo, as no study is able to confirm that saline infiltration is devoid of

Table 2 Summary of secondary outcome data

		n	SMD	CI	P-value
VAS Scores	T0	729	-0.71	-1.16, -0.26	0.002
	T4	558	-0.65	-1.25, -0.06	0.03
	T24	881	-0.52	-0.94, -0.10	0.01
Time to first analgesic request		403	1.18	0.67, 1.69	<0.00001
Intraoperative morphine use		343	-0.55	-1.07, -0.03	0.04
Duration of hospital stay		321	-0.25	-0.48, -0.03	0.03
	PONV	732	OR 0.82	0.49, 1.37	0.44

CI, confidence interval; OR, odds ratio; SMD, standard mean difference; VAS, visual analogue scale.

**Fig 4.** Funnel plot of primary outcome data.

consequences on nociception.^{7,12} The calculated NNT was 3.1 for BSCPb vs saline compared with 14.2 for BSCPb vs no block, but large heterogeneity between the two groups ($I^2=89\%$). This was perhaps because of a smaller number of studies and participants (5/354) in the BSCPb vs no block subgroup compared with (7/681) BSCPb vs saline only block. Hence, these results need to be treated with caution.

Secondary outcome data

Secondary outcome data examining VAS scores in the first postoperative 24 h appear to corroborate primary outcome data. In this analysis, pain scores were significantly improved in the BSCPb cohort at T0, T4, and T24. BSCPb increases the time until first analgesic request by a mean time of 1 h and 44 min ($P<0.00001$). The calculated NNT of 4.4 in favour of BSCPb to reduce the requirement for rescue analgesia in the first 24 h after operation does portend its beneficial effect.

Intraoperative analgesic use demonstrated a statistically significant difference in the quantity of morphine equivalent used when the block was instituted compared with control group (standard mean difference -0.55; 95% CI -1.07, -0.03; $P=0.04$). However, using sensitivity analysis, and excluding the work of Andrieu and colleagues¹⁰ because of their use of clonidine, the intraoperative analgesic use became insignificant ($P=0.13$) indicating that presence of clonidine may have influenced the overall effect. Intraoperative analgesic use was

not statistically different between the preoperative ($n/N=4/182$) ($P=0.05$) and the postoperative BSCPb ($n/N=2/161$) ($P=0.44$) groups. It is unclear as to why there is no discernible difference between the groups, when one would expect the use of analgesic intraoperatively to be lower in the context of pre-incision block. One could speculate that it is perhaps because of the small number of trials and number of patients in both groups as to why we may not observe a difference, dose or timing of premedication, or depth of intraoperative anaesthetic; or a combination of these.

Day-case surgery is becoming increasingly common. In England between 2010 and 2011, 7% of thyroid and parathyroid surgery was performed as a day-case and the mean hospital stay was 2 days.²⁹ In our analysis, the length of hospital stay was significantly reduced in the BSCPb group. This analysis is based on only 321 patients (four studies), and despite reaching statistical significance, has limited clinical implications because of the very small number of studies included and the mean reduction in stay being only approximately 6 h.

PONV is an unpleasant phenomenon that can be a direct determinant of the patient experience.³⁰ In this analysis, the incidence of PONV in the BSCPb group is not statistically different ($P=0.44$). Performing sensitivity analysis by excluding the outlier Suh and colleagues,¹⁶ neither the direction of the overall outcome changes nor does the significance ($P=0.64$). There were trials where scoring of PONV was performed^{11,17} compared with others wherein simple reporting of nausea and vomiting was described,^{10,12,13,16,18,23} which could have accounted for the heterogeneity ($I^2=51\%$) observed. There were not enough trials in the postoperative block group for a subgroup analysis to ascertain the benefit of preoperative block with regards to its effect on PONV.

Comparisons with prior review work

Although Warschkow and colleagues⁵ mention that there was no observed difference in efficacy of administering BSCPb before operation vs after operation, we found that administering the block before operation reduces the use of rescue analgesic (OR 0.25; 95% CI 0.14, 0.45; $P<0.00001$), compared with BSCPb performed after operation (OR 0.56; 95% CI 0.25, 1.25; $P=0.16$). This difference could have arisen because of the small number of studies in the study by Warschkow and colleagues⁵ compared with our study; only eight RCTs including 799 patients. In contrast to Warschkow and colleagues,⁵ however, we found a statistically significant difference between three-point vs two-point technique ($P=0.0004$, $I^2=66\%$). However, in contrast to their study, we found that BSCPb vs saline block ($P<0.00001$) was more effective than BSCPb vs no block/unspecified placebo ($P=0.31$) compared with Warschkow and colleagues.⁵ We assume it might have been because of the limited number of studies and participants in the trial by Warschkow and colleagues⁵ that resulted in the observed differences which might be reflective in their meta regression, wherein they found that there was a correlation between that amount of local anaesthetics used for the BSCPb significantly and the efficacy of the BSCPb. However, the meta-regression performed in our study did not find any correlation between dose of local anaesthetics and efficacy of BSCPb.

In conclusion, BSCPb offers greater analgesic efficacy for postoperative analgesia after thyroid surgery, as evidenced by the NNT=4.4 with an improvement in VAS scores at T0, 4 and 24 h. There is a statistically significant reduction in length of hospital stay but no significant effects on PONV.

Authors' contributions

Conducted and confirmed searches, and included trials into data analysis. Undertook meta-analysis under A.B. supervision. Completed and revised manuscript. Prepared manuscript for submission: D.M.

Conducted initial searches, reviewed trials, conducted Jadad scores and included trials into analysis. Composed first draft of manuscript: N.S., R.K.

Design of study, consultation, review, and editing of manuscript: J.M.H.

Conducted and supervised searches, selected and analysed trials, arbitrated any disputes between other authors. Oversaw manuscript construction and determined overall scientific direction. Supervising author throughout: A.B.

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Declaration of interest

None declared.

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