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Thoracic paravertebral regional anesthesia for pain relief in patients with breast cancer surgery

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Abstract

Background: The present study aimed to assess the efficacy and safety of thoracic paravertebral regional anesthesia (TPVBRA) in patients with breast cancer surgery.

Methods: In total, 72 patients undergoing breast cancer surgery were randomly divided into an intervention group and a control group; each group contained 36 subjects. Both groups received TPVBRA with 20 mL 0.25% bupivacaine. In addition, subjects in the intervention group also received an additional 1 μg/kg dexmedetomidine. Heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), pain intensity (measured by visual analogue scale, VAS), and analgesic consumption were assessed; adverse events were also recorded.

Results: Significant differences were observed in HR ($P < .05$), SBP ($P < .05$), and DBP ($P < .05$) at the 30-minute point during surgery between the 2 groups. In addition, the time of the first administration of analgesia ($P = .043$) and the mean consumption of analgesic agents ($P = .035$) in the intervention group were much better than those in the control group. However, no significant differences in HR or VAS were found at any time point after surgery ($P > .05$). Furthermore, similar adverse events were detected in both groups ($P > .05$).

Conclusion: The results of this study showed that TPVBRA combined with bupivacaine and dexmedetomidine can enhance the duration and quality of analgesia without serious adverse events.

Abbreviations: AEs = adverse events, ASA = American Society of Anesthesiologists, DBP = diastolic blood pressure, HR = heart rate, SBP = systolic blood pressure, TPVBRA = thoracic paravertebral regional anesthesia, VAS = visual analogue scale.

Keywords: breast cancer, bupivacaine, clinical trial, dexmedetomidine, regional anesthesia, thoracic paravertebral block

1. Introduction

Breast cancer is one of the most common cancers in female patients.[1] It is reported that approximately 40% of patients who undergo breast cancer surgery experience significant acute postoperative pain.[2] It is also reported that more than 50% of breast surgery patients suffer from chronic postoperative pain and inadequate analgesia.[3] This type of pain often disturbs patients, which demonstrates that insufficient conventional pain management is available for relief.[2] Therefore, multiple pain management methods are often applied to postoperative pain control.

Thoracic paravertebral regional anesthesia (TPVBRA) appears to be a useful adjunctive intervention for pain management after cancer surgery.[4–7] Previous studies have reported that this intervention was used for pain relief during a variety of post operations, including thoracotomy,[8] mastectomy,[9] and cholecystectomy.[10] It has also reported that patients who received TPVBRA often involved less nausea and vomiting.[5] In addition, it can not only shorten the recovery time, reduce analgesics consumption, but can also decrease total surgery cost.[5] Although the use of TPVBRA can either improve the quality and duration of sensory neural blockade or reduce the consumption dose of local and supplemental analgesia,[11] no systematic review or meta-analysis of TPVBRA for the usage of breast cancer surgery is available presently.

Dexmedetomidine is a highly selective α2 agonist. It has sedative and analgesic properties and produces dose-dependent analgesia without respiratory depression.[12] It has been reported that dexmedetomidine can produce analgesia in experimental animals,[13] prolong the duration of action of spinal bupivacaine,[14] and can potentiate the effect of spinal morphine in patients with cancer pain.[15]

This study aimed to test the hypothesis that the efficacy of TPVBRA combined with bupivacaine and dexmedetomidine is superior to TPVBRA with bupivacaine alone in patients undergoing breast cancer surgery.

2. Material and methods

This randomized controlled trial was approved by the Medical Ethical Committee of The Affiliated Hongqi Hospital of Mudanjiang Medical University, and conducted at this hospital

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from December 1, 2012, to November 30, 2016. Seventy-two patients were included, and were randomly allocated to an intervention group or a control group at a 1:1 ratio. All patients met the inclusion and exclusion criteria and provided written informed consent.

This study included the patients under American Society of Anesthesiologists (ASA) physical status I-III aged from 20 to 70 years, 50 to 80 kg in mass. All patients were scheduled for elective modified radical mastectomy with axillary dissection. Patients were excluded if they were allergic to the study drugs; or had conduction abnormalities, bleeding diathesis, prior breast surgery, neurological disease or psychiatric illness, maternal cardiovascular disease, severe liver or renal diseases, pregnant, or breast-breeding.

The randomization of this study was performed using a SAS 8.1 (SAS Institute, Inc., Cary, NC) computerized number generator, and the assignments were masked to the participants, investigators, outcome assessors, and data analysts in this study.

All participants were recruited from the department of the obstetrics and gynecology at The Affiliated Hongqi Hospital of Mudanjiang Medical University. All patients were randomly divided into an intervention and a control group after confirmation of breast cancer diagnosis. All researchers and investigators were trained before this study.

All patients in both groups received general anesthesia. It was induced by 1.5 μg/kg fentanyl, 2 to 3 mg/kg propofol, and 1.5 mg/kg lidocaine. Endotracheal intubation was facilitated with 0.15 mg/kg cisatracurium. After intubation, anesthesia was maintained using 1 to 1.5 MAC isoflurane. Doses of 0.5 μg/kg fentanyl and 0.03 mg/kg cisatracurium were administered as necessary.

In addition, patients in the control group received 20 mL of 0.25% bupivacaine paravertebrally, which was divided into 3- to 4-mL aliquots in each level. The participants in the intervention group received 20 mL of 0.25% bupivacaine and 1 μg/kg dexmedetomidine paravertebrally, divided into 3- to 4-mL aliquots in each level. The block was administrated over 10 to 15 minutes. The block success was tested by decreased pin prick sensation at the expected dermatomal level. After the block, the patient was immediately placed in the supine position.

Heart rate (HR), systolic blood pressure (SBP), and diastolic blood pressure (DBP) were measured during surgery at 0, 30, 60, and 120 minutes. In addition, HR and pain [using the visual analogue scale (VAS)] were measured and evaluated immediately at 3, 6, 12, 24, 36, and 48 hours after surgery. The time of initial administration and the mean use of analgesic were also evaluated. Adverse events (AEs) after surgery were also recorded.

2.1. Statistical analysis

The estimated sample size was 30 participants in each group; $\alpha = 0.05$ (2-sided) and $\beta = 0.20$. Assuming a 20% dropout rate, at least 72 patients should be recruited for this study, with 36 in each group. All outcome data were analyzed using an intention-to-treat approach. Analysis of variance (ANOVA), Bonferroni, Friedman, and Wilcoxon rank tests with relative risks and 95% confidence intervals were used for data analysis. $P < .05$ was considered significant.

3. Results

Ninety-six patients with breast cancer undergoing surgery were initially recruited (Fig. 1). Twenty-four patients were excluded because they did not meet the inclusion criteria (n = 18) or declined to participate (n = 6). Therefore, 72 patients were included and were randomly divided into an intervention or a control group; each group had 36 patients. Eight patients withdrew from the study before completion (Fig. 1).

The baseline characteristics of all included patients in both groups are summarized in Table 1. No significant baseline differences in patient characteristics of age, body mass index, race, ASA status, or type of surgery were detected between the 2 groups (Table 1).

No significant differences in HR, SBP, or DBP values were found between the 2 groups at all time points, except at the 30-minute point during surgery (Table 2). Moreover, there were not

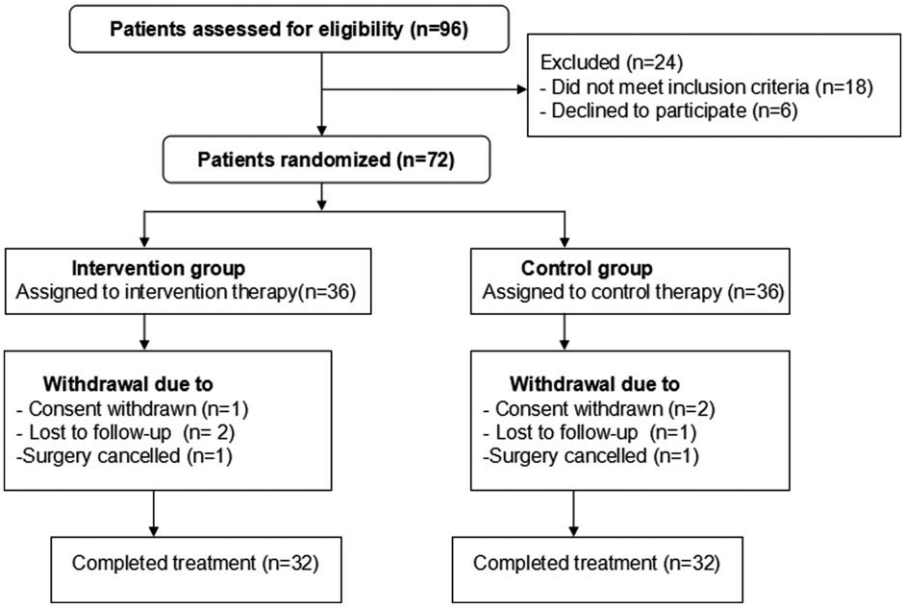

Figure 1. Flow of the participants through the study.

Table 1

Patients characteristics at baseline.

Characteristics	Intervention group (n = 36)	Control group (n = 36)	P
Age, y	57.6 (10.3)	58.8 (11.0)	.63
Body mass index, kg/m^2	27.8 (7.5)	28.0 (7.3)	.91
Race			
Han ethnicity	36 (100.0)	36 (100.0)	1.00
ASA status			
I	13 (36.1)	10 (27.8)	.45
II	19 (52.8)	20 (55.5)	.81
III	4 (11.1)	6 (16.7)	.50
Type of surgery			
Simple mastectomy	10 (27.8)	9 (25.0)	.79
Modified radical	6 (16.7)	6 (16.7)	1.00
Wide local excision/node dissection	19 (52.8)	21 (58.3)	.64
Other	1 (2.7)	0 (0.0)	.49

Note: Data are present as mean ± standard deviation or number (%).
ASA = American Society of Anesthesiologists.

Table 4

Mean time of intravenous analgesia consumption after surgery.

Variables	Intervention group (n = 36)	Control group (n = 36)	P
Time to first request pain medicine, h	8.3 (6.6)	6.4 (5.1)	.043
Tramadol consumption, mg	148.9 (74.8)	195.7 (66.2)	.035

Note: Data are present as mean ± standard deviation.

Table 5

Adverse events between 2 groups.

Adverse events	Intervention group (n = 36)	Control group (n = 36)	P
Nausea	4 (11.1)	3 (8.3)	.69
Vomiting	3 (8.3)	2 (5.6)	.65
Pnemothorax	1 (2.8)	0 (0.0)	.49

Note: Data are present as number (%).

significant differences in HR and VAS at any time point after surgery between the 2 groups ($P > .05$, Table 3). However, there were significant differences in time of initial postoperative administration of the analgesic ($P = .043$) and in the mean analgesic use ($P = .035$) between the 2 groups (Table 4).

Three AEs, nausea, vomiting, and pneumothorax, occurred in this study. However, no significant difference in AEs was found between the 2 groups (Table 5). In addition, no treatment-related deaths were observed in either group.

4. Discussion

Previous studies have reported that the combination of TPVBRA and general anesthesia has a positive effect for patients undergoing breast cancer surgery. One study reported that the adjunctive fentanyl or clonidine to the levobupivacaine (0.05%) has promising effect of analgesics. In addition, such intervention can significantly reduce the consumption of supplemental postoperative morphine in patients with breast cancer surgery.[16] The other study noted that both rescue analgesic consumption and cumulative pain scores were significantly lower at rest and during movement in the treatment groups.[17] Another study demonstrated that the addition of 1 μg/kg dexmedetomidine to 0.25% bupivacaine in thoracic PVB in patients undergoing a modified radical mastectomy improved the quality and duration of analgesia and provided an analgesic sparing effect with no serious side effects.[18] The results of our study are consistent with the previous study.[18]

In this study, we demonstrated that participants who received general anesthesia and TPVBRA with bupivacaine and dexmedetomidine showed superior postoperative analgesia, prolongation of the time to initial rescue analgesic requirement, and decreased total intravenous tramadol consumption compared with patients who received general anesthesia combined with TPVBRA and bupivacaine alone in the first 48 hours after breast cancer surgery.

Although positive results were achieved in this study, it still had several limitations. First, the sample size was quite small, which

Table 2

Outcome measurements in HR, SBP, and DBP during the period of the surgery.

Outcome measurements	Groups	0 min	30 min	60 min	120 min
HR	Intervention	84.1 (6.9)	68.4 (8.3)*	74.6 (10.7)	77.8 (9.8)
	Control	83.5 (6.8)	79.1 (6.6)	80.1 (8.4)	80.3 (8.5)
SBP	Intervention	129.1 (11.6)	102.4 (11.8)*	124.8 (12.2)	127.0 (12.5)
	Control	127.8 (12.3)	120.1 (13.3)	131.9 (12.9)	133.2 (8.7)
DBP	Intervention	81.4 (7.5)	64.9 (7.8)*	75.1 (5.9)	78.0 (7.0)
	Control	81.2 (7.1)	76.4 (7.4)	77.7 (7.6)	77.9 (6.7)

Note: Data are present as mean ± standard deviation.
DBP = diastolic blood pressure; HR = heart rate; SBP = systolic blood pressure.
* P value is significant < .05.

Table 3

Outcome measurements in HR and VAS score after surgery.

Outcome measurements	Groups	0 h	3 h	6 h	12 h	24 h	36 h	48 h
HR	Intervention	77.6 (10.7)	79.5 (10.1)	80.1 (8.5)	83.8 (8.9)	83.1 (8.2)	84.0 (8.2)	84.3 (8.3)
	Control	80.0 (10.5)	81.2 (9.4)	82.8 (7.9)	84.0 (8.1)	84.2 (8.0)	84.5 (7.8)	84.8 (7.6)
VAS	Intervention	2.5 (0.4)	2.2 (0.5)	2.4 (0.5)	2.5 (0.6)	2.4 (0.5)	2.3 (0.4)	2.3 (0.4)
	Control	2.6 (0.4)	2.3 (0.6)	2.5 (0.6)	2.7 (0.7)	2.7 (0.6)	2.6 (0.5)	2.5 (0.6)

Note: Data are present as mean ± standard deviation.
HR = heart rate; VAS = visual analogue scale.

may have affected the results. Second, this study was only conducted at 1 center at The Affiliated Hongqi Hospital of Mudanjiang Medical University, and all patients were of Han Chinese ethnicity, which may influence the generalizability of this finding to other ethnicities and other hospitals. Third, patients also received general anesthesia, which may have affected this study; the observed effect may have been the result of the synergistic effect of general anesthesia with bupivacaine and dexmedetomidine, or of bupivacaine alone.

5. Conclusion

This study found that TPVBRA combined with bupivacaine and dexmedetomidine had a positive effect on anesthesia and had similar safety in breast cancer patients compared with the control treatment. Further studies should include a larger sample size to verify this result.

References

[1] Smith RA, Cokkinides V, Brawley OW. Cancer screening in the United States 2009: a review of current American Cancer Society Guidelines and issues in cancer screening. CA Cancer J Clin 2009;59: 27–41.
[2] Poleshuck EL, Katz J, Andrus CH, et al. Risk factors for chronic pain following breast cancer surgery: a prospective study. J Pain 2006;7: 626–34.
[3] Gartner R, Jensen MB, Nielsen J, et al. Prevalence of and factors associated with persistent pain following breast cancer surgery. J Am Med Assoc 2009;302:1985–92.
[4] Exadaktylos AK, Buggy DJ, Moriarty DC, et al. Can anesthetic technique for primary breast cancer surgery affect recurrence or metastasis? Anesthesiology 2006;105:660–4.
[5] Karmakar MK. Thoracic paravertebral block. Anesthesiology 2001;95: 771–80.
[6] Tahiri Y, de Tran QH, Bouteaud J, et al. General anaesthesia versus thoracic paravertebral block for breast surgery: a metaanalysis. J Plast Recontr Aesthet Surg 2011;64:1261–9.
[7] Schnabel A, Reichl SU, Kranke P, et al. Efficacy and safety of paravertebral blocks in breast surgery: a meta-analysis of randomized controlled trials. Br J Anaesth 2010;105:842–52.
[8] Tamura T, Mori S, Mori A, et al. A randomized controlled trial comparing paravertebral block via the surgical field with thoracic epidural block using ropivacaine for post-thoracotomy pain relief. J Anesth 2017;31:263–70.
[9] Kulhari S, Bharti N, Bala I, et al. Efficacy of pectoral nerve block versus thoracic paravertebral block for postoperative analgesia after radical mastectomy: a randomized controlled trial. Br J Anaesth 2016;117:382–6.
[10] Fentie DY, Gebremedhn EG, Denu ZA, et al. Efficacy of single-injection unilateral thoracic paravertebral block for post open cholecystectomy pain relief: a prospective randomized study at Gondar University Hospital. Local Reg Anesth 2017;10:67–74.
[11] Lin SS, Salinas FV. Continuous plexus and peripheral nerve blocks for postoperative analgesia. Anesth Analg 2003;96:263–72.
[12] Khan ZP, Ferguson CN, Jones RM. (2 and imidazoline receptor agonists: their pharmacology and therapeutic role. Anaesthesia 1999;54:146–65.
[13] Stevens C, Brenner G. Spinal administration of adrenergic agents produces analgesia in amphibians. Eur J Pharmacol 1996;316:205–10.
[14] Kanazi GE, Aouad MT, Jabbour-Khoury SI, et al. Effect of low-dose dexmedetomidine or clonidine on the characteristics of bupivacaine spinal block. Acta Anaesthesiol Scand 2006;50:222–7.
[15] Ugur F, Gulcu N, Boyaci A. Intrathecal infusion therapy with dexmedetomidine supplemented morphine in cancer pain. Acta Anaesthesiol Scand 2007;51:388.
[16] Barlacu CL, Frizelle HP, Moriaty DC, et al. Fentanyl and clonidine as adjunctive analgesics with levobupivacaine in paravertebral analgesia for breast surgery. Anaesthesia 2006;61:932–93.
[17] Bhuvaneswari V, Jyotsna W, Preethy JM, et al. post-operative pain and analgesic requirement after paravertebral block for mastectomy: a randomized controlled trial of different concentrations of bupivacaine and fentanyl. Indian J Anaesth 2012;56:34–9.
[18] Mohamed SA, Fares KM, Mohamed AA, et al. Dexmedetomidine as an adjunctive analgesic with bupivacaine in paravertebral analgesia for breast cancer surgery. Pain Physician 2014;17:E589–98.