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Adding Dexmedetomidine to Methylene Blue in Thoracic Paravertebral Block for Video-Assisted Lobectomy: A Case Series Study

Francesco Coppolino, Simona Brunetti, Leonardo Maria Bottazzo, Gianluigi Cosenza, Pasquale Sansone, Marco Fiore, Maria Beatrice Passavanti, Vincenzo Pota, Maria Caterina Pace

Department of Women, Children and General and Specialized Surgery, University of Campania Luigi Vanvitelli, Naples, Italy

Correspondence: Simona Brunetti, Department of Women, Children and General and Specialized Surgery, University of Campania Luigi Vanvitelli, Piazza Luigi Miraglia N.2, Naples, 80134, Italy, Tel +3934924241O8, Email simona.brunetti@studenti.unicampania.it

Purpose: Thoracic surgery often results in severe chronic postoperative pain. Current evidence favors two locoregional techniques. Thoracic Epidural Anesthesia (TEA), the gold standard, and Thoracic Paravertebral Block (TPVB), which is associated with fewer side effects but is limited by short duration of action of local anesthetics (LA) and potential failure due to improper drug distribution. This study investigates the use of dexmedetomidine (DEX) as adjuvant to prolong the effects of LA in TPVB, with methylene blue used for visual confirmation of accurate injectate spread.

Patients and Methods: We observed 6 patients undergoing Video-Assisted Thoracoscopy (VATS) lobectomy who received TPVB with ropivacaine, DEX and methylene blue. The primary endpoint was postoperative pain recorded at 1, 12, 24, 48 hours using Numeric Rating Scale (NRS); the secondary endpoints were cumulative opioid consumption in the first 24 hours in Milligram Morphine Equivalents (MME); adverse events: occurrence of bradycardia, hypotension, Postoperative Nausea and Vomiting (PONV); length of hospital stay. All patients completed the study.

Results: Our results showed optimal pain scores, with NRS scores always below 4, decreased need for opioids, and prolonged analgesia. None of the patients had bradycardia nor PONV, but two patients experienced acute and self-limited hypotension following TPVB.

Conclusion: Thoracic Paravertebral Block with Dexmedetomidine and methylene blue was effective and safe in controlling post-operative pain. Methylene blue could help improving knowledge on anesthetics distribution to reduce failure rates.

Keywords: locoregional anesthesia, paravertebral block, post-operative pain, thoracic surgery

Introduction

Thoracic surgery can generate severe pain that often persists beyond the acute postoperative period, challenging recovery, and rehabilitation.[1] Systemic analgesia alone is not sufficient for adequate pain control. Locoregional anesthesia provides several beneficial effects including optimal pain control and decreased need for opioids; it also reduces postoperative nausea and vomiting (PONV) and other complications, improving recovery and shortening hospital stay.[2] Two locoregional approaches have been broadly validated for chest surgery analgesia: the thoracic epidural anesthesia (TEA) considered the gold standard, and the Thoracic Paravertebral Block (TPVB).[3] Current literature comparing TEA and TPVB has evidenced how both share similar analgesic efficacy.[4] However, TPVB is associated with fewer adverse events, as hypotension and postoperative nausea and vomiting.[5]

TPVB[6] conveys anesthesia to the paravertebral space, a virtual area communicating with the epidural space through the intervertebral foramen, the intercostal neurovascular space, the sympathetic chain, and the parietal pleura. All these structures are believed to be involved in nociceptive transmission during thoracic surgery. Intercostal nerves in this area are devoid of perineural fascia which makes them more susceptible to local anesthetics (LAs) action. Injection of LAs

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induces somatic and sympathetic anesthesia across several thoracic dermatomes, the extent of which is determined by the spread of the LAs, which can be difficult to predict. The main contraindications for TPVB include patient refusal, hypersensitivity to LA, coagulation disorders or oral anticoagulant use (INR> 1.4), infection or mass infiltrating the injection site, respiratory infection or empyema, chest deformity.[7]

The TPVB can be used for both anesthesia and analgesia in case of thoracic, cardiac, breast, upper abdominal surgery, and even in chronic pain conditions.[8–10]

The efficacy of TPVB relies upon correct identification of the injection site, and failure may be intimately connected to inappropriate distribution of the injected drug.[11] As TPVB usually requires higher volumes of LAs to ensure sufficient anesthetic coverage compared to TEA, well-aimed distribution of LAs may as well allow reduction of LAs doses, lowering potential side effects related to overdosage. Moreover, the efficacy of TPVB is limited by the normal duration of action of the LA, which is particularly relevant in the postoperative period. Many solutions have been explored to extend duration of local anesthesia[12] including placement of catheter for continuous infusion of LAs. This however requires additional time and costs and increases the risks of infections and neurological complications. Numerous substances have been added to LAs to prolong their duration of action with varying efficacy,[13] including opioids, adrenergic substances[14,15] and steroids.[16] Among these, dexmedetomidine (DEX) recently came under the spotlight: DEX is a highly selective alpha-2 adrenergic receptor agonist with sedative and analgesic properties with no effects on the GABA receptor.[17] It has sympatholytic and opioid sparing effects.[18,19] Peripheral analgesic effects of DEX are likely dependent on reduction in the release of norepinephrine and independent inhibition of nerve fibers action potentials via the alpha-2 receptor. The efficacy and safety of DEX combined with LAs has been widely studied in current literature as it significantly prolongs and potentiates analgesic efficacy, without clinically relevant side effects.[20,21] However, there is little information about the effectiveness of DEX combined with LAs in TPVB. We therefore performed a case-series to assess the safety and efficacy of DEX combined with LAs in TPVB. In our study TPVB was performed through addition of methylene blue to the anesthetic mixture to verify in the immediate intraoperative time the correct localization of the injectate, a technique that was tested by Agnoletti et al with satisfactory results.[22]

Material and Methods

We hereby present a series of 6 patients (age range 66–81; 3F and 3M; BMI 18–22) scheduled for VATS lobectomy in our institution between October 2023 and March 2024 undergoing removal of lung cancer. Exclusion criteria were: hypersensitivity to drugs used in the study; history of thoracic surgery; psychiatric disorders; conversion to thoracotomy; contraindications to TPVB; intravenous infusion of DEX; lack of written consent; participation to other studies.

Patients were observed since hospital admission until discharge. Demographic data was recorded (age, sex, BMI) along with clinical history and intraoperative variables (heart rate, blood pressure).

The primary endpoint was pain experienced in the first two postoperative days at 1, 12, 24, 48 hours using Numeric Rating Scale (NRS) ranging from 0 to 10 (from absence of pain to worst imaginable pain).

Secondary endpoints were: opioids consumption, measured as cumulative consumption in the first postoperative day in Milligram Morphine Equivalents (MME); adverse events: occurrence of bradycardia, hypotension evidenced by a reduction in MAP of more than 20% from the baseline and PONV; length of hospital stay (days).

All patients followed the same anesthetic protocol; none were excluded during the study.

Patients received preoperative unilateral TVPB with a solution of 20 mL containing ropivacaine 0.5% plus DEX 1μg/kg plus methylene blue 1% and normal saline. The block was performed through percutaneous landmark identification and under ultrasound-guide to locate the paravertebral space, at vertebral level T3-T4 or T4-T5. The needle was inserted perpendicular to the skin, approximately 3 cm lateral to the spinous process, advanced until contact was made with the transverse process. The needle was then retracted cephalad and redirected towards the paravertebral space, slowly advanced until a loss of resistance is encountered, approximately 1 cm inferior to the transverse process. After negative aspiration, a 3-mL test dose of the anesthetic mixture was injected; the remainder was subsequently administered in a single bolus.

General anesthesia was then induced with propofol 2mg/kg and fentanyl 100 μg bolus, maintained with desflurane.

Table 1 Postoperative Pain Evaluation and Opioid Consumption

NRS Pain Scores:	1	2	3	4	5	6	Average
1st hour	0	4	2	3	7	3	3
12th hour	0	2	1	2	6	2	2
24th hour	0	2	1	2	5	2	2
48th hour	0	1	0	1	3	1	1
Total opioid consumption in 24h (mg)				14.2 ± 2.8			

Thoracoscopy was then begun and allowed first visualization of correct spread of the anesthetic mixture. Absence of blue dye inside the chest was considered failed TPVB; in these cases, the block was repeated at the end of the surgery using the same technique. Postoperative analgesia consisted in paracetamol 1 gram IV every six hours, and ketorolac 30 mg IV if NRS was above four. Rescue analgesia in case NRS was still > 4 was tramadol 50 mg intravenously.

Results

Postoperative pain scores on average were inferior to 4 in all time periods. In the first postoperative hour NRS ranged from 0–7 (on average 3); in the 12th hour NRS range was 0–6 (on average 2); in the 24th hour NRS ranged between 0 and 5(on average 2); in the 48th hour NRS range was 0–3 (on average 1). Cumulative opioid consumption in the first 24 hours was 14.2 ± 2.8 mmEs. (Table 1) All patients were alive during our observation time. The length of hospital stay was on average 5.8 days.

Two patients had hypotensive episodes following TPVB; however, in all cases the hypotension briefly resolved after intravenous administration of a bolus dose of vasopressor drug ephedrine. We did not observe any other severe hypotensive episodes intraoperatively. No episodes of bradycardia nor PONV have occurred after TPVB.

Discussion

Our results indicate that DEX in methylene blue TPVB can be a safe and reliable analgesic technique for unilateral surgical trunk procedures. This approach improves postoperative pain scores, extends the duration of analgesia, and reduces cumulative postoperative analgesic consumption. Additionally, methylene blue provides an immediate visual depiction of local anesthetic spread of TPVB. (Figure 1) While altered tissue coloration might hinder from correct identification of vascular structures, no complications related to this was observer in our study. The methylene blue spreading patterns confirmed findings by Naja et al[23] who identified four different patterns via radiographic assays: pure longitudinal, longitudinal + intercostal, intercostal, and cloud-like.

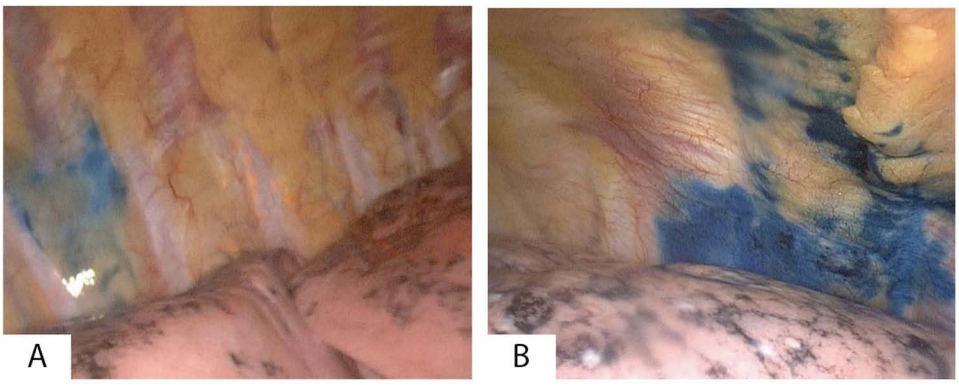

Figure 1 Two cases of methylene blue PVB (**A**): Methylene blue at T5 during right upper lobectomy. (**B**): Methylene blue at T4-T5 during left upper lobectomy.

Several technical variations of TPVB have been explored to enhance its efficacy. It can be performed percutaneously, either blindly via surface landmark identification or under ultrasound guidance; alternatively, surgeons can inject LAs under direct visualization. The technique has proven feasible, with high success and relatively low complication rates. Naja et al reported failure of the technique of percutaneous needle insertion block to be 6.1% in adults.[24] In a subsequent study,[25] the use of nerve stimulators, fentanyl and clonidine improved the technique, extending its duration. Some studies compared single vs multiple injections, reporting the former as most effective.[26] Recently, fluoroscopic confirmation,[27,28] pressure measurement techniques,[29] direct visualization of catheter placement approach,[30,31] have been described in literature. Despite the positive results, their superiority over simple ultrasound-guided TPVB remains unclear.

In our study, methylene blue provided an immediate and unmistakable confirmation of anesthetic spread. Beyond its colorimetric function, methylene blue may offer additional benefits from its antioxidant and anti-inflammatory properties. Studies on post-herpetic neuralgia have shown satisfactory analgesic efficacy and safety of methylene blue in TPVB as single injections[32] or continuous infusion.[33] Zhao and colleagues found that methylene blue TPVB significantly reduced plasma levels of inflammatory markers as IL-6, TNF-α and cortisol. Further investigations are needed, but these findings suggest that methylene blue could potentially mitigate the damages related to the surgical stress response.

The analgesic efficacy of the technique may also be attributed to adjuvant DEX. Recent studies have investigated the use of DEX as adjuvant in TPVB for thoracic surgery. The addition of dexmedetomidine to TPVB with local anesthetics appears to significantly reduce postoperative opioid consumption and pain scores, especially during coughing.[34–36] This combination also improved postoperative pulmonary functions and patient satisfaction without serious side effects. During VATS, adjuvant DEX TPVB prolonged the duration of postoperative analgesia.[36] Furthermore, the combination of TPVB and intravenous dexmedetomidine infusion for medical thoracoscopy demonstrated comparable efficacy to general anesthesia, with lower patient-rated procedural pain scores and higher operator-rated satisfaction scores.[37] These findings suggest that dexmedetomidine is a valuable adjunct to TPVB for thoracic procedures, and were further confirmed in the review by Wang et al[38] demonstrated that DEX with LAs in TPVB improved postoperative pain scores and opioid consumption in several surgeries including breast, thoracic and abdominal. An increased incidence of hypotension was also observed. In our study, no severe bradycardia was noted, but post-procedural hypotension did occur, and was treated with bolus vasopressors. Hemodynamic stability was quickly restored and maintained throughout the intraoperative and postoperative period, and surgery was carried out in absence of other complications. The impact of this finding should be explored on a larger scale, as current ERAS guidelines after lung surgery tend to support TPVB over TEA also based on the occurrence of hypotension.[39]

Correct perioperative analgesia is essential for recovery and prevention of chronic pain syndromes,[40,41] as Post-Thoracotomy Pain Syndrome (PTSP). PTSP has a prevalence between 33% and 91%, can result from rib trauma, intercostal nerve compression, or muscle inflammation. It is often difficult to treat due to both nociceptive and neuropathic components.[42,43] It has been treated with opioids and non-opioid medications like gapentinoids, often unsuccessfully, as emerged in a recent study.[44] Studies have shown that VATS is associated with lower incidence of PTPS compared to thoracotomy, yet it still occurs in 29.3% of patients. Maloney et al[45] highlighted the role of younger age in the development of this condition, indicating the need to further investigate on age-related differences in TPVB safety and efficacy. One study by Gong et al[46] comparing ultrasound guided TPVB to general anesthesia found significant improvement in pain scores, opioid consumption and hospital stay for TPVB, with fewer side effects, particularly urinary retention. Interestingly, no significant inter-age differences in safety and efficacy were found, an important finding for elderly patients who are more vulnerable to complications and opioid-related side effects. Urinary retention was not assessed in our study, as the focus was on hypotension and PONV.

This pilot study was performed in a single center, which ensured uniformity in surgical and anesthetics practices, but limited its external validity. Additionally, the small sample size reduces generalizability of the results. Larger multicenter studies with stratification of age and BMI are necessary to validate our results. A recent trial[47] has found a positive correlation between increasing BMI and pain scores and opioid consumption. Obesity poses challenges for execution of the procedure and perioperative management of comorbidities. Obese patients are more susceptible to opioid related side effects and postoperative dyspnea.

Conclusions

The use of methylene blue in combination with Dexmedetomidine and Local Anesthetics in Thoracic Paravertebral Blocks for Video-Assisted Thoracoscopy lobectomy seemed to provide adequate analgesia in the first postoperative hours, reducing opioid consumptions and the length of hospital stay. We did not observe bradycardia or Post-operative Nausea and Vomiting, but only two episodes of acute post-procedural hypotension. A larger study sample is deemed necessary to power the study.

Abbreviations

PONV, Postoperative Nausea and Vomiting; TEA, Thoracic Epidural Anesthesia; TPVB, Thoracic Paravertebral Block; LA, Local Anesthetic; VATS, Video-Assisted Thoracoscopy; DEX, Dexmedetomidine; NRS, Numeric Rating Scale; MME, Milligram Morphine Equivalents.

Data Sharing Statement

The published information is available from the corresponding author on reasonable request.

Ethics Approval and Consent to Participate

The authors declare no conflicts of interest. This study was conducted in accordance with the ethical standards set forth by the Declaration of Helsinki. Prior to the initiation of the research, ethical approval was obtained as required from the Medical and Ethics Committee of the Università degli Studi della Campania "Luigi Vanvitelli" – Azienda OspedalieraUniversitaria "Luigi Vanvitelli" – AORN "Ospedale dei Colli" (trial approval number 0032765/i).

Consent for Publication

Written informed consent was obtained from the patients, as required by our institution (Università degli Studi della Campania Luigi Vanvitelli) which also granted approval for publication of the case report and accompanying images.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that they have no competing interests.

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