A comparison of port-site infiltration with bupivacaine alone vs. bupivacaine plus dexmedetomidine after diagnostic staging laparoscopy
Rabeea Sajid Qureshi, Tanveer Alam, Huma Saleem

Abstract
Objective: To compare the effects of bupivacaine alone and in combination with dexmedetomidine following staging laparoscopies.
Method: This triple-blinded, prospective study was conducted from June to September 2021 at a tertiary care cancer hospital in Lahore, Pakistan, and comprised adult patients having American Society of Anaesthesiologists grade I-III, weighing >30kg and undergoing diagnostic staging laparoscopy. The subjects were randomised into two equal groups. Group A received 6ml of 2mg/kg bupivacaine at each of the four laparoscopic port sites before skin closure, while group B additionally received 2µg/kg dexmedetomidine. The presence and severity of pain were recorded and assessed at 15 min, 1, 2 and 4 hours as well as at the time of discharge from the post-anesthesia care unit. The time to first request for rescue analgesia, total morphine consumption, and the occurrence of any side effects during their stay were also recorded. Data was analysed using SPSS 23.
Results: Of the 30 patients, 15(50%) were in group A; 10(66.6%) males and 5(33.3%) females with mean age 43.27±7.59 years. There were 15(50%) patients in group B; 12(80%) males and 3(20%) females with mean age 41.36±12.42 years (p>0.05). Of the total, 29(96.66%) patients were classified as American Society of Anaesthesiologists grade II, and 1(3.33%) patient in group A was grade III. There was no significant difference between the groups in any of the outcome measures assessed (p>0.05), and none of the patients experienced any side effect throughout the post-operative stay.
Conclusion: The combination of dexmedetomidine and bupivacaine had no significant improvement in pain relief compared to bupivacaine alone.
Keywords: Diagnostic laparoscopy, Staging laparoscopy, laparoscopy, Dexmedetomidine, Bupivacaine, Local infiltration, Regional anaesthesia. (JPMA 74: 857; 2024) DOI: https://doi.org/10.47391/JPMA.8483

Introduction
In 2020, 1.9 million new cases worldwide were estimated to be affected by colorectal cancer, almost 1 million by gastric cancer and 604,100 by oesophageal cancer.1 Diagnostic staging laparoscopy (DSL) is a minimally invasive surgery performed to identify and/or disprove local, regional or metastatic extension of malignancies, determine the feasibility of the proposed curative cancer surgery, and facilitate obtaining biopsy specimens, cultures and aspiration.2 The smaller surgical incision prevents the morbidity and mortality associated with laparotomy.

Effective postoperative analgesia is essential in preventing various detrimental metabolic or cardiovascular effects as well as hormonal changes, like adrenocorticotropic hormone, cortisol and prolactin, that occur in response to surgical stress.3 Intravenous (IV) opioids are a commonly used modality for postoperative analgesia, but they may induce sedation, delayed gastrointestinal (GI) motility, nausea, vomiting or respiratory depression, all of which can lead to a delay in discharge from the hospital.4 Other proposed methods include the use of non-steroidal anti-inflammatory drugs (NSAIDs), regional neuraxial techniques or nerve blocks. However, regional blocks may be contraindicated in several patients. On top of that, they also require a certain degree of expertise in skills in order to be performed effectively.

Peri-incisional local anaesthetic infiltration has been suggested as an effective and opioid-sparing analgesic technique.5,6 Long-acting local anaesthetics, like bupivacaine, alone provide analgesia for up to 2-8 hours.7 This will usually lead to reoccurrence of pain during the patient’s post-anaesthesia care unit (PACU) stay or during night time, hindering their sleep. In order to extend the duration of local anaesthetic action and prolonged comfort of the patients, adjuncts maybe used simultaneously.

Dexmedetomidine is a selective alpha (α)2-adrenoceptor agonist approved by the United States Food and Drug Administration (FDA) for continuous IV sedation in intensive care settings. It has been safely used via epidural and intrathecal routes8 as well as for IV regional
A comparison of port-site infiltration with bupivacaine alone vs. bupivacaine plus dexmedetomidine following DSLs. The null hypothesis was that the addition of dexmedetomidine to bupivacaine would attenuate postoperative opioid requirement, delay postoperative pain in the patients.

**Patients and Methods**

The triple-blinded, prospective study was conducted from June to September 2021 at Shaqukat Khanum Memorial Cancer Hospital and Research Centre, Lahore, Pakistan. After approval form the institutional ethics review board, the sample size was calculated using an online resource in the light of an earlier study while keeping power of study 90% and α-error not exceeding 0.05. The sample size was inflated to compensate for any unexpected dropouts.

The study included American Society of Anaesthesiologists (ASA) physical status I-III patients aged 18-70 years, weighing at least 30kg who were scheduled to undergo elective laparoscopic staging surgery. Patients with ASA IV and above, those with a known history of hypersensitivity to the study drugs, any significant cardiac, respiratory, renal or hepatic comorbidities, coagulation disorders, infection in the vicinity of the surgical wound, or any psychiatric illness that may interfere with perception and assessment of pain were excluded. Patients whose surgical technique required insertion of >4 ports or who had any other event that interrupted routine surgical procedure leading to non-routine interventions and those who refused to participate in the study were also excluded.

To ensure blind allotment and eliminate bias, an online randomiser was used, and a list of serial numbers was generated to divide the sample into two equal groups. Patients were allocated sequentially as they presented for surgery such that the first patient was No. 1 and so on. Patients were allocated sequentially after taking written informed consent as they presented for surgery. Exclusion of a patient would allocate their random number to the next patient without alteration in the original randomisation list. Control group A received 24ml of 2mg/kg bupivacaine divided equally for four laparoscopic port sites, while those in intervention group B received 24ml of 2mg/kg bupivacaine plus 2µg/kg of dexmedetomidine divided equally for four trocar sites.

The dosage calculation was done based on lean body mass, and the anaesthetic solution was prepared in a sterile syringe by an anaesthetist not involved in the subsequent stages of the study. All the participating patients, surgeons, their attending anaesthetists, data collectors and data analysts were blinded to the identity of the study drug infiltrated for postoperative analgesia. The patients were briefed preoperatively about rating their pain using the Numerical Rating Scale (NRS), scoring 0 for ‘no pain’ and 10 for ‘the worst pain imaginable by the patient’.

Intraoperatively, standard monitors, including electrocardiography (ECG), non-invasive blood pressure (NIBP), pulse oximetry and capnography, were used. No anxiolytics were given. General anaesthesia induction was done with IV 0.1mg/kg morphine, 1-2mg/kg propofol, and 0.5mg/kg atracurium to facilitate intubation. Anaesthesia was maintained with sevoflurane in 50% oxygen/air mixture. Atracurium boluses were repeated as required. All the patients were given 1g paracetamol IV and 4mg ondansetron for postoperative nausea and vomiting prophylaxis 15min before the end of the procedure. Neuromuscular blockade was reversed with neostigmine/glycopyrrolate prior to extubation. The prepared drug syringe was handed over to the surgeon after they removed the trocars, who then administered the contents at the port sites (6ml for each site) using a 20-gauge needle, before extubating the patient. It was ensured that the surgeon had >4 years of professional experience.

After transferring the patient to PACU with standard monitoring, the presence and severity of pain was assessed using NRS by the registered nurse attending the patient. The values were recorded at 15 min, 1 hour, 2 hours, 4 hours and at the time of discharge from PACU. The time to first request for rescue analgesia was also noted, and patients were given 2mg morphine IV in such cases. This dose was repeated if and when required. Total morphine consumption was recorded. The presence of side effects, like nausea, vomiting, hypotension, bradycardia, sedation, respiratory depression and psychological complications, was observed throughout the PACU stay.

Data was recorded on a predesigned proforma and was analysed using SPSS 23. Continuous variables were presented as median with interquartile range (IQR) and were analysed using Mann-Whitney U test. Categorical data was presented as frequencies and percentages, and was analysed using chi-square or Fisher’s exact test, as...
appropriate. Pain scores were analysed using Kruskal-Wallis test and Mann-Whitney U test. \( p \leq 0.05 \) was considered significant.

**Results**

Of the 30 patients, 15(50%) were in group A; 10(66.6%) males and 5(33.3%) females with mean age 43.27±7.59 years. There were 15(50%) patients in group B; 12(80%) males and 3(20%) females with mean age 41.36±12.42 years \( (p>0.05) \). Of the total, 29(96.66%) patients were classified as American Society of Anaesthesiologists grade II, and 1(3.33%) patient in group A was grade III (Table 1).

There were 8(53.33) patients in each group who requested for rescue analgesia \( (p>0.05) \). The time to first request for rescue analgesia and median dose of morphine were not significantly different between the groups (Table 2).

Median NRS scores were not significantly different between the groups (Table 3).

None of the patients experienced any pain >4 hours after PACU transfer and at the time of discharge. Also, there was no side effect in any of the patients.

**Table-1: Descriptive data.**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Group A</th>
<th>Group B</th>
<th>( p )-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)* Mean±SD</td>
<td>43.27±7.59</td>
<td>41.36±12.42</td>
<td>0.669</td>
</tr>
<tr>
<td>ASA Grade** n (%)</td>
<td>II 14 (93.33)</td>
<td>15 (100)</td>
<td>&gt;0.999</td>
</tr>
<tr>
<td>Gender** n (%)</td>
<td>Male 10 (66.66)</td>
<td>12 (80)</td>
<td>0.635</td>
</tr>
<tr>
<td>Total Dose of Morphine Administered (mg)**</td>
<td>4 (2)</td>
<td>2 (0)</td>
<td>0.672</td>
</tr>
</tbody>
</table>

Table-2: Inter-group comparison related to rescue analgesia.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Group A</th>
<th>Group B</th>
<th>( p )-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Request for Rescue</td>
<td>Yes 8 (53.33)</td>
<td>8 (53.33)</td>
<td>&gt;0.999</td>
</tr>
<tr>
<td>Analgesia* n (%)</td>
<td>No 7 (46.66)</td>
<td>7 (46.66)</td>
<td></td>
</tr>
<tr>
<td>Time for First Request (min)**</td>
<td>5 (15)</td>
<td>10 (15)</td>
<td>0.835</td>
</tr>
<tr>
<td>Median (IQR)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total Dose of Morphine Administered (mg)**</td>
<td>4 (2)</td>
<td>2 (0)</td>
<td>0.672</td>
</tr>
<tr>
<td>Median (IQR)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table-3: Inter-group comparison related to pain scores at various time points.

<table>
<thead>
<tr>
<th>Pain Score (NRS)* (Median (IQR))</th>
<th>15 min</th>
<th>1 hour</th>
<th>2 hours</th>
<th>4 hours</th>
<th>Discharge</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group A</td>
<td>4 (4)</td>
<td>0 (3)</td>
<td>0 (0)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Group B</td>
<td>0 (2)</td>
<td>0 (2)</td>
<td>0 (0)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>( p )-value</td>
<td>0.66</td>
<td>0.425</td>
<td>0.582</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

**Discussion**

As an adjuvant in locoregional anaesthesia, dexmedetomidine is known to cause a dose-dependent improvement in block quality, reduction in the dosage and prolongation of the duration of neural blockade produced by the local anaesthetics.\(^{18}\) This potentiation is mediated by \( \alpha-2 \) receptor agonism that inhibits nerve fibre action potentials and, hence, the transmission of pain signals by diminishing the release of noradrenaline.\(^9\)

Previous studies\(^{19,20}\) have regarded incisional pain as the most conspicuous pain following laparoscopy. Strategies for pain relief following outpatient minor surgical procedures, such as DSL, typically include opioid derivatives in addition to NSAIDs and/or paracetamol. Nevertheless, with recent evidence urging opioid-sparing techniques to aid rapid recovery and avoid the potential side effects or unplanned postoperative admissions, wound infiltration with local anaesthetics appears to be a safe and effective modality for analgesia given the simple skill set required.\(^{20-24}\)

A meta-analysis in 2021 analysed 23 randomised controlled trials (RCTs) to establish the efficacy of local anaesthetics with added dexmedetomidine.\(^{25}\) It reported significantly prolonged time to first rescue analgesia and reduction in rescue analgesia, analgesic consumption, as well as postoperative pain scores. This meta-analysis included the trials which corroborated the results in laparoscopic cholecystectomy patients.\(^ {14,15}\)

In view of the aforementioned evidence, it is safe to assume that utilising dexmedetomidine in conjunction with a long-acting local anaesthetic drug, like bupivacaine, would prove to be more efficacious. The current study, however, did not exhibit any significant difference in the choice of local anaesthetic solution infiltrated, and adding dexmedetomidine to bupivacaine did not prove to be superior to using bupivacaine alone. Although the time to request for rescue analgesia and average pain scores were seemingly higher in the patients who were given plain bupivacaine solution at the incision, the differences did not reach statistical significance. None of the current patients developed any noteworthy side effects associated with the use of \( \alpha-2 \) agonists. Moreover, the results were contrary to the previous studies that found significant reduction in opioid consumption and improvement in pain scores using dexmedetomidine as an adjunct.\(^ {9-15}\) One relevant factor worth considering is that all the previous studies investigated patients undergoing surgical procedures involving some form of resection, while the current subjects underwent only a diagnostic laparoscopy.

The key strength of the current study was its triple-blinded
design. The methodology ensured minimal bias and random allocation of participants. Additionally, the infiltration technique was uniform throughout the cohort, and was only performed by surgeons with >4 years of professional experience.

The current study had its limitations because we did not follow up with the patients beyond PACU, which would have been beneficial in drawing a conclusion regarding the more long-lasting pain relief between the two groups. Also, the lack of patients with higher ASA grades calls for further caution in the extrapolation of the results to all patients. More extensive studies may be helpful in confirming any added advantage of dexmedetomidine as an adjunct to local anaesthetics.

Conclusion
The combination of dexmedetomidine and bupivacaine had no significant improvement in pain relief compared to bupivacaine alone.

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Conflict of Interest: None.

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References


Author Contribution:
RSQ: Study concept, design, data analysis, interpretation, drafting.
TA: Study concept, design, questionnaire design, data collection.
HS: Study design, supervision.