Spinal vs General Anesthesia for Laparoscopic Cholecystectomy

Interim Analysis of a Controlled Randomized Trial

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Objective: To compare spinal anesthesia with the gold standard general anesthesia for elective laparoscopic cholecystectomy in healthy patients.

Design: Controlled randomized trial.

Setting: University hospital.

Patients: One hundred patients with symptomatic gallstone disease and American Society of Anesthesiologists status I or II were randomized to have laparoscopic cholecystectomy under spinal (n=50) or general (n=50) anesthesia.

Methods: Intraoperative parameters, postoperative pain, complications, recovery, and patient satisfaction at follow-up were compared between the 2 groups.

Results: All the procedures were completed by the allocated method of anesthesia, as there were no conversions from spinal to general anesthesia. Pain was significantly less at 4 hours (P<.001), 8 hours (P<.001), 12 hours (P<.001), and 24 hours (P=.02) after the procedure for the spinal anesthesia group compared with those who received general anesthesia. There was no difference between the 2 groups regarding complications, hospital stay, recovery, or degree of satisfaction at follow-up.

Conclusions: Spinal anesthesia is adequate and safe for laparoscopic cholecystectomy in otherwise healthy patients and offers better postoperative pain control than general anesthesia without limiting recovery.

Trial Registration: clinicaltrials.gov Identifier: NCT00492453


Surprisingly, in the era of minimally invasive medicine, regional anesthesia has not gained popularity and has not been routinely used as a sole method of anesthesia in laparoscopic procedures. Johnson noted that “all laparoscopic procedures are merely a change in access and still require general anesthetic; hence the difference from conventional surgery is likely to be small.” This statement is predominantly based on the assumption that laparoscopy necessitates endotracheal intubation to prevent aspiration and respiratory embarrassment secondary to the induction of carbon dioxide pneumoperitoneum, which is not well tolerated in a patient who is awake during the procedure. However, it is surprising that regional anesthesia has been successfully used for laparoscopic cholecystectomy in patients unfit to have the procedure under general anesthesia.
but has not been tested in healthy patients in whom any presumed risk would be theoretically much lower. Hamad and Ibrahim El-Khattary\textsuperscript{7} used spinal anesthesia for laparoscopic cholecystectomy for the first time in a small series of healthy patients. In their study, however, nitrous oxide pneumoperitoneum was applied instead of the standard carbon dioxide.

We have recently shown the feasibility of successfully and safely performing laparoscopic cholecystectomy with low-pressure carbon dioxide pneumoperitoneum under spinal anesthesia alone in healthy patients with symptomatic gallstone disease.\textsuperscript{8} We have also noticed that spinal anesthesia results in exceptionally minimal postoperative pain. After this pilot study, we designed a controlled randomized trial to compare spinal anesthesia with the gold standard general anesthesia for elective laparoscopic cholecystectomy in healthy patients.

**METHODS**

From September 2004, all patients referred to our unit for elective laparoscopic cholecystectomy were considered eligible for the trial, provided that they fulfilled the following inclusion criteria: American Society of Anesthesiologists’ status I or II, between 18 and 65 years of age, body mass index (calculated as weight in kilograms divided by height in meters squared) of 30 or less, and normal coagulation profile. Exclusion criteria were acute cholecystitis, pancreatitis or cholangitis, previous open surgery in the upper abdomen, contraindication for pneumoperitoneum, and contraindication for spinal anesthesia owing to spinal deformity. Informed consent was obtained from all patients and the trial protocol was approved by the institutional ethics committee.

Patients were randomized to have a laparoscopic cholecystectomy under either general or spinal anesthesia. Randomization was created by a computer-generated list in blocks of 20 patients with sex stratification. Numbered and sealed envelopes were placed in the operating room and only opened at the patients’ arrival there, so that both the patient and involved physicians were unaware of the randomization arm beforehand. The primary end point of the trial was any difference in postoperative pain between the 2 groups, and the secondary end points were differences in complication rate, hospital stay, recovery, and patient satisfaction. A sample size of 150 patients per randomization arm was calculated on an expected 20% difference in the postoperative pain assessed by the visual analog scale between the 2 groups, with a power of 80% at detecting this difference at the 5% level. We planned to perform an interim analysis after the first 100 patients and the results of this analysis are discussed.

Patients’ preoperative evaluation and preparation were standardized. All patients received deep venous thrombosis prophylaxis (20 mg of enoxaparin sodium subcutaneously once a day) during hospitalization. Both anesthesia and surgery were performed in all cases by the same anesthetic and surgical team. On patients’ arrival in the operating room, after establishing noninvasive monitoring (electrocardiogram, arterial blood pressure, and pulse oximetry), an arterial line was inserted for the purpose of the study (for direct blood pressure monitoring and blood sampling) and 500 mL of Ringer solution was commenced intravenously. All patients were intravenously administered 1 mg of midazolam hydrochloride, 3 mg of granisetron hydrochloride, and 30 mg of ranitidine hydrochloride before the induction of anesthesia. A nasogastric tube was also inserted (to be removed at the end of the procedure in both groups for methodological reasons) to decompress the stomach and avoid vomiting and aspiration; this is especially useful for the spinal group.\textsuperscript{8} After obtaining baseline vital signs, oxygen at 5 L/min was commenced through a face mask.

Patients randomized to spinal anesthesia were positioned at the right lateral decubitus position and a 25-gauge pencil-point spinal needle was introduced into the subarachnoid space at the L2-L3 intervertebral space under aseptic conditions. After free flow of cerebrospinal fluid was obtained, 3 mL of hyperbaric bupivacaine hydrochloride, 0.5%, 0.25 mg of morphine, and 20 µg of fentanyl citrate were injected intrathecally. Then, the patient was placed in the supine position, staying in the Trendelenburg position for 3 minutes. If the mean arterial blood pressure decreased by more than 20% below the preanesthetic value, an intermittent intravenous infusion of phenylephrine hydrochloride solution, 0.004%, was initiated and titrated to effect.

The anesthesia was continued with sevoflurane, 1% to 2%, and atracurium besylate (0.5 mg/kg). Balanced anesthesia was continued with sevoflurane, 1% to 2%, and propofol (2 mg/kg/h). After intubation of the trachea, the lungs were ventilated with 50% oxygen in air using a semiclosed circle system. Ventilation was controlled with a tidal volume of 8 to 10 mL/kg and the ventilatory rate was adjusted to maintain a PaCO\textsubscript{2} value of 35 to 40 mm Hg. Residual neuromuscular block was antagonized with 25 µg of neostigmine methylsulfate and 1 mg of atropine sulfate at the end of surgery.

All patients were monitored continuously during the operation. Both clinical observation and invasive hemodynamic monitoring (electrocardiogram, heart rate, arterial blood pressure, respiratory rate, pulse oximetry, arterial blood gas, and acid-base balance) were recorded at 5-minute intervals, except PaCO\textsubscript{2} (15-minute intervals). Laparoscopic cholecystectomy was performed by using the same technical principles for both groups, with the standard 4-trocar technique as previously described.\textsuperscript{4} Pneumoperitoneum was established by using the open (Hasson) technique with carbon dioxide at a maximum intra-abdominal pressure of 10 mm Hg, instead of the usual 14 mm Hg. Another modification of the technique was the minimal—if any—tilting of the operating table, ie, head up and left tilt to minimize diaphragmatic irritation.

Operative time as well as any intraoperative events were recorded. Specifically, for patients having spinal anesthesia, and thus being alert during the procedure, we recorded any symptoms related to either the anesthetic approach or the pneumoperitoneum, such as shoulder pain, headache, nausea, and discomfort. Drainage of the subhepatic space was not used.

Postoperatively, all patients were given standard intravenous fluids (1 L of Ringer solution and 1 L of dextrose, 5%, for the next 24 hours) and intravenous analgesia (40 mg of parecoxib sodium every 12 hours, 500 mg of acetaminophen every 6 hours, and supplementary opioids on demand). Postoperative pain was assessed at both relaxed and stressed (ie, after coughing) conditions by using the visual analog scale at 4, 8, 12, and 24 hours after the completion of the procedure. Other postoperative events related either to surgical or (especially) anesthetic procedure, such as discomfort, nausea and vomiting, shoulder pain, urinary retention, pruritus, headache, and other neurologic sequelae, were also recorded. The patients were fed orally the morning after the operation and discharged 24 hours after the procedure, unless complications had occurred.

All patients were followed up 10 to 15 days after the operation as outpatients by an independent physician who was not involved in the procedure and was blinded to patients’ type of
anesthesia to assess their recovery and degree of satisfaction with the procedure by using a standardized questionnaire. This included a questionnaire, tailored to the relevant procedure, regarding quality of life assessment during the first 2 weeks after the operation. Questions targeted the severity of pain during patients' recovery period; how this influenced their daily activities; the type, amount, and duration of analgesia required; the degree of satisfaction from the anesthetic procedure and the whole process; as well as their final impressions compared with their initial expectations. The answers were scored, with a total score ranging from 0 to 26. Another telephone contact was performed at 1 month postoperatively to detect late complications.

Statistical analysis was performed using the Arcus QuickStat Biomedical statistical package (Research Solutions, Cambridge, England). The Mann-Whitney U and Fisher exact tests were used as appropriate to detect differences between the 2 groups. Differences were considered significant at \( P < .05 \) (2-tailed test).

### RESULTS

Between September 2004 and September 2006, 100 patients entered our ongoing trial. They were randomized to have laparoscopic cholecystectomy under spinal (\( n = 50 \)) or general (\( n = 50 \)) anesthesia. One patient from the spinal anesthesia arm withdrew informed consent, and in 2 patients from the general anesthesia arm, the laparoscopic procedure was converted to an open approach. These 3 patients were therefore excluded from further analysis, leaving 49 patients in the spinal and 48 patients in the general anesthesia groups for analysis (Figure).

The 2 groups were similar regarding demographics (Table 1). All the procedures were completed by the allocated method of anesthesia, as there were no conversions from spinal anesthesia to general anesthesia. Intraoperatively, intravenous phenylephrine was administered in 29 (59%) patients from the spinal anesthesia arm in comparison with 12 of the 48 (25%) patients who received general anesthesia. However, the pain was severe enough to require intravenous fentanyl administration in only 10 cases. The remaining patients did not require any additional medication or other intervention, and procedures were completed uneventfully in all cases.

Discharge from the hospital at 24 hours after surgery was possible for 48 (98%) patients from the spinal anesthesia group and 47 (98%) patients from the general anesthesia group. We had no mortality in either group and essentially no major morbidity. One patient from the regional anesthesia group who required catherization for urinary retention developed a urinary tract infection and was treated with antibiotics, and 1 patient from the general anesthesia group was readmitted on day 10 with thoracic pain. This patient was found to have peripheral pulmonary embolism and was treated with anticoagulants. Workup for potential risk-factor detection revealed protein C deficiency.

Postoperative events related to surgical and/or anesthetic procedures, like nausea, vomiting, or urinary retention, are presented in Table 2. As presented in Table 3, pain assessed by the visual analog scale was significantly less for the spinal anesthesia group at 4, 8, 12, and 24 hours postoperatively, including both relaxed and stressed conditions. Supplementary postoperative opioid analgesia was administered in only 1 of the 49 (2%) patients who received spinal anesthesia compared with 12 of the 48 (25%) patients who received general anesthesia (\( P < .001 \), Fisher exact test).

At 2 weeks’ follow-up, the quality of life and patient satisfaction scores were similar in the 2 groups: patients who received spinal anesthesia had a median score of 19...
avoidance of endotracheal intubation–related discomfort; the presence of adequate levels of analgesia for the first few hours after the completion of the surgical procedure owing to the existing activity of the analgesia injected in the subarachnoid space; and the potentially minimal stress response associated with a minimal invasive anesthetic procedure, such as spinal anesthesia.\(^8,9\) Pain following laparoscopic cholecystectomy is not a major problem, but it has been a matter of interest in several studies during the last few years. Minimal invasive surgery has dominated because of the rapid and smooth recovery it offers, and postoperative pain control is probably the main factor that characterizes smooth recovery. Several researchers have tested intraperitoneal instillation or aerolization of local anesthetic agents (eg, bupivacaine), use of the newer anti-inflammatory COX-2 inhibitors (ie, parecoxib, which was used in this study), addition of epidural analgesia, and oral or epidural administration of steroids, finding some effect on postoperative pain, which varies between studies.\(^3,10-14\) When we designed this trial comparing the 2 methods of anesthesia on several aspects of the intraoperative and postoperative course, we defined postoperative pain control as our primary end point based on the initial experience gained from our pilot study,\(^9\) in which the exceptionally good postoperative pain control became obvious very quickly. Our data presented herein confirm the superiority of spinal over general anesthesia in postoperative pain control.

Intraoperative events of note in the spinal anesthesia group included a decrease of the mean arterial blood pressure of more than 20% below the preanesthetic value as well as right shoulder pain. With regards to the former, this is a well known adverse effect of spinal anesthesia and is easily overcome after administration of phenylephrine, and therefore it does not essentially affect the planned procedure. Regarding the latter, 43% of the patients who received spinal anesthesia experienced some degree of shoulder pain or discomfort; however, less than half of those patients required treatment. Laparoscopy-related right shoulder pain has been reported in previous studies and attributed to diaphragmatic irritation from carbon dioxide pneumoperitoneum.\(^5,7\) At times, this symptom could be severe enough to result in conversion of the anesthetic approach.\(^7\) However, the pain was mild in most cases in our study and it did not result in conversion from spinal anesthesia in any of our patients. Even when present, shoulder pain was easily dealt with; reassurance and no medical treatment were used in most patients who experienced this symptom. This could be attributed to our lower cutoff pressure for pneumoperitoneum (10 mm Hg instead of the usual 14 mm Hg) combined with minimal tilting of the operating table; we have, thus, minimized the diaphragmatic irritation. A potentially useful maneuver to overcome this minor drawback in the future could be the intraperitoneal aerosolization with local anesthetic agents like bupivacaine before the induction of pneumoperitoneum, which has been shown recently to significantly reduce postoperative shoulder tip pain.\(^11\)

As mentioned before, we have chosen a low-pressure pneumoperitoneum at a maximum of 10 mm Hg to

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**Table 2. Postoperative Adverse Events in Patients Who Underwent Laparoscopic Cholecystectomy**

<table>
<thead>
<tr>
<th>Postoperative Event</th>
<th>Received Spinal Anesthesia (n = 49)</th>
<th>Received General Anesthesia (n = 48)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea/vomiting</td>
<td>7</td>
<td>8</td>
</tr>
<tr>
<td>Dizziness</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Pruritus</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Urinary retention</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Sinus rhythm tachycardia</td>
<td>0 (0-1)</td>
<td>1 (0-1)</td>
</tr>
</tbody>
</table>

**Table 3. Pain Scores in Patients Who Underwent Laparoscopic Cholecystectomy**

<table>
<thead>
<tr>
<th>Test Condition</th>
<th>Visual Analog Scale Score, Median (Range)</th>
<th>(P) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>At 4 hours</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Resting</td>
<td>0 (0-4)</td>
<td>3 (0-8)</td>
</tr>
<tr>
<td>Stress</td>
<td>2 (0-8)</td>
<td>5 (1-10)</td>
</tr>
<tr>
<td>At 8 hours</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Resting</td>
<td>0 (0-6)</td>
<td>2 (0-7)</td>
</tr>
<tr>
<td>Stress</td>
<td>2 (0-7)</td>
<td>5 (0-8)</td>
</tr>
<tr>
<td>At 12 hours</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Resting</td>
<td>0 (0-2)</td>
<td>2 (0-7)</td>
</tr>
<tr>
<td>Stress</td>
<td>1 (0-7)</td>
<td>4 (0-7)</td>
</tr>
<tr>
<td>At 24 hours</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Resting</td>
<td>0 (0-4)</td>
<td>1 (0-6)</td>
</tr>
<tr>
<td>Stress</td>
<td>1 (0-7)</td>
<td>2.5 (0-7)</td>
</tr>
</tbody>
</table>

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The interim analysis of our study not only confirmed the feasibility of safely performing laparoscopic cholecystectomy under spinal anesthesia as the sole anesthetic procedure but also showed the superiority of spinal anesthesia in postoperative pain control compared with the standard general anesthesia. Pain assessed at both relaxed and stressed conditions was significantly lower at any time during the postoperative hospital stay in patients having spinal anesthesia compared with those having general anesthesia. Furthermore, supplementary opioids were administered in significantly fewer patients having spinal anesthesia compared with those having general anesthesia. This difference could be attributed to a combination of several factors: the

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**COMMENT**

(range, 4-26) compared with a median score of 20 (range, 6-26) for patients who received general anesthesia \(P = .2\), Mann-Whitney \(U\) test). Overall, 96% of the spinal anesthesia group and 94% of the general anesthesia group were highly or fairly satisfied with the anesthetic procedure they had. No late complications were reported at week 4 through telephone contact in any of the patients.
minimize diaphragmatic irritation. The use of low-pressure pneumoperitoneum did not jeopardize the adequacy of our space—and subsequently the view—and virtually all the procedures were completed without any technical difficulty. This is especially true for the spinal anesthesia group, because this type of anesthesia offers sensory, motor, and sympathetic blockade at a high level and thus obviates the need for abdominal wall muscle relaxants, which sometimes are necessary when general anesthesia is used. To avoid technical problems with obese patients in whom a potentially higher intra-abdominal pressure is required, we designed the trial with a body mass index cutoff of 30. It is possible, however, that carefully selected patients with higher body mass indexes could have laparoscopic cholecystectomy under regional anesthesia, as our limited anecdotal experience with such obese patients outside the trial suggests.

With regards to the early (in-hospital) postoperative course, the only essential event detected in the spinal anesthesia group was urinary retention; again, this is known to be related to regional anesthesia with rates of up to 20% in some series. Postoperative urinary retention developed in 3 (6%) patients from the spinal anesthesia group (1 female and 2 male patients). Instant catheterization was the only treatment required in 2 patients and did not affect their recovery or time of discharge. However, the third patient developed a postcatheterization urinary tract infection requiring antibiotics and prolonged hospitalization. At 2 weeks’ follow-up, the vast majority of patients from both groups reported being satisfied with the anesthetic approach and experienced equally good recovery.

To our knowledge, this is the fist controlled randomized trial that compares the application of spinal with general anesthesia in “the average” patient who undergoes elective laparoscopic cholecystectomy with carbon dioxide pneumoperitoneum. Our data so far have confirmed the preliminary results of our pilot study regarding the feasibility and safety of spinal anesthesia for this purpose. Moreover, it appears that spinal anesthesia is more effective than the standard general anesthesia on postoperative pain control during the patient’s hospital stay. On the other hand, postdischarge patients’ recovery after laparoscopic cholecystectomy under spinal anesthesia was reported to be equally good compared with the present standard method of anesthesia. From these preliminary data, it appears that spinal anesthesia is a promising method of anesthesia for laparoscopic procedures, and with proper refinements, it could potentially evolve as the new gold standard anesthetic approach for elective laparoscopic cholecystectomy in healthy patients.

Accepted for Publication: January 21, 2007.
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Financial Disclosure: None reported.

REFERENCES