Comparison of General Anesthesia with Spinal Anesthesia in Laparoscopic Cholecystectomy Operations

Laparoskopik Kolesistektomi Ameliyatlarında Genel Anestezi ile Spinal Anestezinin Karşılaştırılması

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ABSTRACT

Objective: Laparoscopic cholecystectomy (LC) operations are being performed under general anesthesia (GA). Further studies are needed on the issue whether these operations can be performed under spinal anesthesia (SA). In this study we aimed to compare SA with (GA) in terms of efficacy and complications in patients who will undergo LC operations, and to investigate the effects of preemptive analgesia on the development of shoulder pain, transition to general anesthesia, and postoperative analgesia.

Methods: ASA I-II risk group between 18-65 years of age undergoing laparoscopic cholecystectomy were randomly divided into general anesthesia (GA, n=30) and spinal anesthesia (SA, n=30) groups. Patients were premedicated with i.v. midazolam and fentanyl preoperatively. Anesthesia was induced with propofol in the GA group, and maintained with desflurane and remifentanil. In the SA group, spinal anesthesia was provided with intrathecal administration of 15 mg bupivacaine at L2-3 level, and block level was increased to T4 by keeping the patient in Trendelenburg position for 7-10 minutes. Demographic data, hemodynamic parameters, operation time, visual analog scale (VAS) scores at postoperative 0th, 1st, 4th, 8th, 12th and 24th hours, patient-surgeon satisfaction, side effects, and occurrence of right shoulder pain in SA group were recorded.

Results: Effective anesthesia was produced in both groups. Hypotension was observed in 5, bradycardia requiring atropine administration in 4, and perioperative shoulder pain in 9 patients in Group SA, but none of them required general anesthesia. Hypotension developed in one patient in Group GA. The postoperative VAS scores were significantly lower in Group SA at 0th, 1st, 4th hours. Patient satisfaction scores were higher in Group SA.

Conclusion: We concluded that spinal anesthesia may be an alternative method to general anesthesia in patients who will undergo laparoscopic cholecystectomy operations especially when the risk of general anesthesia is too high.

Keywords: Laparoscopic cholecystectomy, general anesthesia, spinal anesthesia, surgeon satisfaction, postoperative pain

ÖZ

Amaç: Laparoskopik kolesistektomi (LK) operasyonları yaygın olarak genel anestezi altında uygulanmaktadır. Spinal anestezi ile bu operasyonları yapılıp yapmamaya konusunda daha fazla çalışmayı ihtiyaç duymaktadır. Bu çalışmadada LK geçirecek olgulara genel anestezi ile spinal anestezinin etkinlik ve komplikasyonları açısından karşılaştırılmış ve uygulanmış preemptif analjezinin omuz ağrısını, genel anestezinin geç bırakmayı ve postoperatif anestezi analjezi üzerinde olan etkilerinin araştırılması amaçlanmıştır.

Yöntem: Laparoskopik kolesistektomi uygulanacak 18-65 yaş aralığında, ASA I-II risk grubunda 60 hasta, rastgele, genel anestezi (Grup GA, n=30) ve spinal anestezi (Grup SA, n=30) olarak iki gruba ayrıldı. Her iki grupta operasyon öncesinde i.v. midazolam ve fentanil ilave olarak verildi. GA grubunda propofol ile anestezi indüksiyonu sonrası desflurane ve remifentanil ile devam edildi. SA grubunda ise spinal anestezi L2-3 aralığında girilerek 15 mg bupivakain ile spinal anestezi sağlandı. Uygun gerilim ve kestirme için Trendelenburg pozisyonuna girdiler. Anestezi sonrası saniyeler içinde hemodinamik değişiklikler, uygulanan analjez ve yan etki kaydedilerek karşılaştırıldı. SA grubunda peroperatif sağ omuz ağrısı sorgulanarak kaydedildi.

Bulgular: Grup SA'da 5 hasta hipotansiyon, 4 hasta atropin verildi, 9 hasta peroperatif plazma pH değeri düşürülürdü. SA grubunda ise 9 hasta peroperatif omuz ağrısı görüldü. Hipotansiyon ve hipotansiyon sırasında gelişen yan etkiler sorgulanmadı. Postoperatif VAS skorları Grup GA'da sırasıyla 0.1, 4.8, 12. ve 24. saatte spinal anestezi ile spinal anestezi arasında anlamlı bir fark saptanmadı.

Sonuç: Laparoskopik kolesistektomi geçirecek hastalarda, özellikle genel anestezi riskinin yüksek olduğu durumda, spinal anestezinin genel anestezinin alternatif bir yöntem olarak kabul edilmektedir.

Anahtar kelimeler: Laparoskopik kolesistektomi, genel anestezi, spinal anestezi, cerrah memnuniyeti, postoperatif ağrı
INTRODUCTION

Laparoscopy has been used in cholecystectomy operations since 1988 in patients with symptomatic cholelithiasis, and has been the first choice of surgical method with time. This technique has been preferred because of its less invasiveness, shorter hospital stay and shorter return to daily activities, and reduced postoperative pain1. While laparoscopic cases are traditionally performed under general anesthesia recent studies have shown that neuroaxial blocks may be good alternatives in these surgeries2. Studies have reported that achievement of anesthesia between T4 to T6 level in neuroaxial blocks is sufficient for these operations3,4. In addition spinal anesthesia has been shown to yield more favourable outcomes than general anesthesia in terms of postoperative pain, complications, and procedural costs5,6. However, during pneumoperitoneum in patients having spinal anesthesia some side effects are encountered related to insufflations of the abdominal cavity. The shoulder pain is one of these complications which is caused by the irritation of the subdiaphragmatic area with CO₂, and reported to be seen in 25% of laparoscopic cases performed under spinal anesthesia. This area is innervated by phrenic nerve originating from 3rd to 5th cervical nerve roots. Normally this level is not blocked, and the pain can not be prevented in conventional spinal anesthesia applications7. Postoperative pain is another problem in these patients. The cause of this pain is multifactorial but the visceral pain is prominent. Preemptive analgesia can be provided by reducing central sensitization of noxious stimuli by spinal anesthesia. The transition to general anesthesia was reported to be inevitable in 3.4% of the cases. However, studies about the effects of spinal anesthesia in cholecystectomy operations have not yielded satisfactory results yet.

In this study we aimed to compare the effectiveness of spinal anesthesia with that of general anesthesia in laparoscopic cholecystectomy operations, and to evaluate the effects of preemptive analgesia on the development of shoulder pain, on the rate of transition to general anesthesia, and on postoperative analgesia.

MATERIALS and METHODS

This study approved by the Istanbul Medeniyet University Goztepe Training and Research Hospital, Clinical Studies Ethics Committee, on December 30 2016, with decision number 2016/0223. Informed consent was taken from the patients enrolled in this study.

Sixty patients in ASA I and II risk groups aging between 18-65 years and undergoing elective laparoscopic cholecystectomy were included in the study. Patients in ASA III risk group or above, and over 65 or under 18 years of age, with local anesthetic or opioid allergy, active infection or abnormal coagulation tests, who were contraindicated for spinal anesthesia, and those who could not be cooperated were excluded from the study. We randomly divided the patients into two groups as spinal anesthesia (Group SA, n=30) and general anesthesia (Group GA, n=30) groups using computer generated random list. The cardiac rhythm, heart rate (HR), noninvasive blood pressure [(systolic (SAP), diastolic (DAP), mean arterial pressure (MAP)], and peripheral oxygen saturation (SpO₂) were monitored. Patients were premedicated with midazolam (25-30 µg/kg IV) in group GA after intravenous catheter insertion. Then, we used 2-2.5 mg/kg propofol and 0.6 mg/kg rocuronium bromide i.v. for anesthetic induction after preoxygenation with 100% O₂ for 2-3 minutes. Patients were ventilated with a tidal volume of 7 ml/kg and a frequency of 12/min. General anesthesia was maintained with 50% O₂/air mixture in 5-6% desflurane and remifentanil i.v. infusion at a dose of 0.5 µg/kg/min. For spinal anesthesia group; after proper positioning, 15 mg Bupivacaine were injected into the subarachnoid space from the L2-3 level with 25 G pencil-point spinal needle (Egemen International, Izmir, Turkey) under sterile conditions. The patients were placed in the su-
pine and at 15-30 degree head down position for about 7-10 minutes, and the analgesia level was expected to rise to T4 level in the control with a pinprick test. The patient was then placed in a light head-up position, and sedation with 25-30 µg/kg i.v. midazolam, and 1 µg/kg fentanyl i.v. was performed as preemptive analgesia, and surgical procedure was started. Ephedrine (10 mg) was planned to be given in case of hypotension (MAP <60 mmHg), and repeated after 5 minutes if it persists. Atropine sulphate (0.5 mg i.v.) was planned to be given in case of bradycardia (HR <40 bpm). Age, gender, ASA risk group, operation time, ephedrine and atropine consumption were recorded. Hemodynamic measurements (SAP, DAP and MAP), oxygen saturation, side effects, and shoulder pain were recorded prior to the procedure (after intubation in Group GA and after drug administration in Group SA) and at 5-minute intervals during the operation. In case of shoulder pain additional fentanyl 1 µg/kg was planned to be given intravenously, and the response was recorded.

In patients having spinal anesthesia the need for nasogastric catheterization, the development of organ damage, hemorrhage or shoulder pain, and lack of response despite the addition of fentanyl were considered as the indication for a transition to general anesthesia. Tramadol 1.5 mg/kg i.v. and metoclopramide i.v. were administered to general anesthesia group patients 10 minutes before the end of surgery. Visual analogue scale (VAS) scores were recorded at the postoperative 0th, 1st, 4th, 8th, 12th and 24th hours in both groups. In the postoperative period tenoxicam i.v. (Oksamen-L 20 mg, Mustafa Nevzat Pharmaceuticals, Istanbul, Turkey) was administered as analgesic drug to patients with VAS values above 4 in both groups. Patients were followed up for the development of postoperative nausea and vomiting (PONV). Since urinary retention was expected after spinal anesthesia, the patients in Group SA were followed up for this complication during postoperative period. For the measurement of patient satisfaction at the postoperative 24th hour, patients in both groups were asked to score the satisfaction level between 0 and 10 in terms of anesthetic technique. The surgeons were also asked to give a score between 0 and 10 for each group in terms of the surgical procedure and comfort, and the both of the scores of the surgeons and patients were recorded.

For statistical analysis, NCSS (Number Cruncher Statistical System) 2007 (Kaysville, Utah, USA) program was used. In the study data, using descriptive statistical methods (mean, standard deviation, median, frequency, ratio, minimum, maximum) quantitative data were compared. For the comparison of the parameters showing normal distribution we used "Student t-Test", and Mann Whitney U par test was used for the comparison of the parameters with non-normal distribution. Pearson’s chi-Square test and Fisher’s exact test were used to compare qualitative data. For intragroup pairwise comparisons of non-normally distributed parameters, “Friedman Test” and “Wilcoxon Signed Ranks” test were used. According to the post-hoc analysis based on the 4th hour VAS values, the effect size was calculated as 1.897, and statistical power as 100% (Open Epi Version 3). Significance was set at P<0.05.

RESULTS

There was no statistically significant difference between groups in terms of age, ASA scores, and operation times (p>0.05). Male/female ratio in spinal anesthesia group, but female/male ratio in general anesthesia group were found to be significantly higher (Table 1). There was a statistically significant difference between Groups GA and SA in terms of body weight (BW) which was significantly higher in Group SA (p=0.048). However, since the difference between the values was less than 10% and p value was close to the threshold, intergroup difference was considered as clinically insignificant.
At baseline and 5th min. after the procedure (induction in the general anesthesia group, and after the block in spinal anesthesia group) there was no statistically significant difference between the groups in HR values, but in the spinal anesthesia group the HR values at 10th min (p=0.002), 15th min (p=0.007), 20th min (p=0.020), and 25th min (p=0.044) after the procedure were significantly lower than Group GA. The HR in group SA was significantly higher than that of Group GA at 45th minute after the procedure (p=0.011). Heart rates were found to be lower in the spinal anesthesia group at 10th, 15th and 20th minutes after the procedure compared to the initial values (p values respectively p=0.005, p=0.038, p=0.002). No statistically significant difference was found between the groups in terms of changes in the HR values before during and after pneumoperitoneum (p>0.05).

After spinal anesthesia, MAP values were lower in the Group SA in between postoperative 15th (p=0.025) and 20th-45th minutes (p<0.001) compared to the Group GA. Significant decreases in MAP values between 5th and 20th minutes were recorded in Group SA compared to baseline. Significant decreases were also noted in MAP values during and after pneumoperitoneum compared to pre-pneumoperitoneum in Group SA. There was a significant intragroup decrease in MAP at the 5th, 10th and 20th min. in Group GA compared to the baseline values (p values respectively p=0.002, p=0.036 and p=0.04). Similarly, blood pressures during pneumoperitoneum were significantly lower than those measured before and after pneumoperitoneum in Group GA (p=0.018). The decrease in MAP values after pneumoperitoneum compared to pre-pneumoperitoneum period in spinal anesthesia group were found to be greater than that of general anesthesia group (p=0.018) (Figure 1).

![Mean Arterial Pressure (MAP)](image1)

*Figure 1. Changes in mean arterial blood pressure values in two groups.*

![VAS Score](image2)

*Figure 2. Changes in visual analogue scale (VAS) values in two groups.*
VAS scores in Group SA were lower in the first four hour than that of general anesthesia group (p<0.001). There was no statistically significant difference between the groups in VAS scores at 8th, 12th and 24th hours postoperatively (Figure 2). No statistically significant difference was found in VAS scores between the genders at any measurement time (p>0.05). There was no difference between the groups in terms of surgical satisfaction scores. Patient satisfaction scores were found to be higher in spinal anesthesia group (p<0.001, Table 2). Shoulder pain was observed in 9 patients (30%) in Group SA. Atropine was given to four patients (13.3%) in Group SA, and not needed in any patient in Group GA (p>0.05). However, there was a statistically significant difference between the groups regarding the use of ephedrine (50% in SA group and 3.3% in GA group, p=0.001, Table 2). SpO2 level did not decrease below 95% in any patient in any group in any period. Post-lumbar puncture headache, urinary retention and PONV have not been observed in any patient.

Table 2. Comparison of side effects between groups.

|                      | Group SA | Group GA | p Value |
|----------------------|----------|----------|---------|
| Surgeon satisfaction score | Min-Max (Median) | Min-Max (Median) | -0.623 |
| Patient satisfaction score | Min-Max (Median) | Min-Max (Median) | -0.001* |
| Shoulder Pain (%) | YES | 21 (70.0) | 26 (86.7) | -0.112 |
| NO | 9 (30.0) | 4 (13.3) | 0 (0) |
| Atropine (%) | YES | 15 (50.0) | 15 (50.0) | -0.001* |
| NO | 30 (100) | 0 (0) | 1 (3.3) |
| Ephedrine (%) | YES | 0 (0) | 30 (100) | NS |
| NO | 30 (100) | 30 (100) | |
| Urinary retention (%) | YES | 0 (0) | 0 (0) | NS |
| NO | 30 (100) | 30 (100) | |
| PONV (%) | YES | 0 (0) | 0 (0) | NS |
| NO | 30 (100) | 30 (100) | |

aMann Whitney U test, bPearson Chi-Square Test, cFisher’s Exact Test, d*p<0.05

Group SA: Group Spinal Anesthesia, Group GA: Group General Anesthesia

DISCUSSION

The main finding of this study is that both anesthetic techniques, namely, general and spinal anesthesia, produced effective, comfortable and safe conditions for laparoscopic surgery. Other important result is that in spinal anesthesia group hypotension and bradycardia were observed at a higher rate, although they did not cause any increase in postoperative complication rate or hospital stay. Lower VAS values in early postoperative period in spinal anesthesia group were also important. Shoulder pain was a problem in Group SA, but it was treated properly, and no patient required general anesthesia. Patient satisfaction was higher in the spinal anesthesia group. Surgeons did not mention any difference between groups in terms of surgical satisfaction.

Bradycardia is an expected side effect due to rapid peritoneal stretch and vagal stimulation in laparoscopic cholecystectomy operations. Bradycardia is observed also in spinal anesthesia in most of the cases due to the inhibition of T1-4 cardiac accelerator fibers and decreased right atrial filling. However, studies have reported that this condition can be prevented by fluid replacement and vasopressor addition. Turkstani et al. reported that 8% of the spinal anesthesia group had bradycardia requiring atropine injection. We obtained similar results in our study.

Hypotension was reported to occur in 20-30% of the patients who underwent spinal anesthesia. However, all patients have responded to fluid replacement and single dose vasopressor therapy. The decrease in the MAP of more than 30% in our study may be related to the fact that the intraabdominal pressure (14 mmHg) applied in our study was higher than the intraabdominal pressure (8-10 mmHg) applied in other studies. Another reason for the higher rate of hypotension in our study may related to higher doses of the drug. However, in another study with low dose thoracic spinal anesthesia, durations of motor and
sensorial block were found to be shorter compare to higher dose used group which may be accept-
ed as an advantage for this type of surgery\textsuperscript{18}.

One of the major intraoperative problems of lap-
aroscopic cholecystectomy under spinal anesthe-
sia is right shoulder pain. Previous studies have
shown that maintaining intra-abdominal pressure
below 10 mmHg reduces right shoulder pain and
respiratory distress due to diaphragm irritation\textsuperscript{19,21}.
In our study, although we routinely applied se-
dation with midazolam and fentanyl to prevent
shoulder pain and restlessness in all patients in
Group SA, 30\% of the patients had mild and short-
term right shoulder pain. In one study, 35.5\% of
the spinal anesthesia group had right shoulder
pain. Of these, 8.9\% had mild and transient shoul-
der pain, 22.2\% required fentanyl, and 4.4\% had
right shoulder pain that did not relieve despite
the addition of fentanyl, and caused a transition
to general anesthesia\textsuperscript{11}. In a study performed with
300 patients laparoscopic surgery was started un-
der spinal anesthesia, and 87.3\% of the patients
had right shoulder pain\textsuperscript{15}. In 90.03\% of the pa-
tients with shoulder pain, the pain was success-
fully treated with massage, and only 9.93\% of the
patients received additional 100 mg tramadol.
However, in 0.67\% of the patients, the surgeon
switched to general anesthesia. In a retrospective
study of 3492 patients who had spinal anesthesia,
12.29\% had shoulder or neck pain. A transition to
general anesthesia was required in 0.004\% of the
patients despite sedoanalgesia\textsuperscript{16}. In our study, in-
traabdominal pressure (14 mmHg), which may be
the reason for the high rate of shoulder pain, was
higher than the intraabdominal pressure applied
in other studies. However, the pain was mild and
disappeared in a short time which we suppose to
be related to fentanyl injection, and conversion to
general anesthesia due to shoulder pain was not
required in any patient.

Although the exact cause of pain after laparoscop-
ic cholecystectomy is still not fully understood, it
is more likely to be multifactorial. Abdominal trau-
ma during insertion of the trocar, diaphragmatic
irritation due to CO\textsubscript{2} insufflation, temperature and
structure of the insufflated gas, intraabdominal
pH, low amount of gas in the peritoneum, intra-
abdominal trauma during the removal of the gall-
bladder out of the abdomen, small tears in the
parietal peritoneum, abdominal distention and
chemical irritation of the peritoneum may be the
causes of this pain\textsuperscript{21-23}. According to the study by
Samer et al.\textsuperscript{11} VAS scores at the 2\textsuperscript{nd} - 4\textsuperscript{th}
hours were lower in the spinal anesthesia group com-
pared to the other group. In another study the
VAS score at the 6\textsuperscript{th} hour was lower in the spi-
nal anesthesia group, but there was no difference
in the VAS scores at the postoperative 12\textsuperscript{th} and
24\textsuperscript{th} hours\textsuperscript{17}. In our study, VAS scores were lower
in the spinal anesthesia group than the general
anesthesia group in the first 4 hours, but no sig-
nificant difference was found in the subsequent
VAS scores. These results are consistent with the
literature. However, the 6\textsuperscript{th} hour VAS score has
not been investigated, and this may be one of the
limitations of our study.

The time of discharge was reported to be shorter
in spinal anesthesia patients, in previous stud-
ies in general, than the general anesthesia group
patients\textsuperscript{4,12,13}. In our study all of the patients were
discharged on the 1\textsuperscript{st} day postoperatively. In fact,
the patients with spinal anesthesia were allowed
to be discharged earlier but they were kept in the
hospital for 24 hours for surgical considerations.

Patient satisfaction is an important factor for mak-
ing decision about the type of anesthesia to be
performed. In a previous study patients in the spi-
nal anesthesia group were reported to be largely
satisfied with the technique of anesthesia. In the
same study 26 patients from the general anesthe-
sia group reported a high degree of satisfaction,
and 3 reported that they were reasonably satis-
fied\textsuperscript{12}. These results are similar to the results of
our study for the Group SA. Higher VAS scores in
the early postoperative period may be respon-
sible from this lower satisfaction rate.
The surgical satisfaction scores were similar in groups in our study. In a previous study, surgical conditions and muscle relaxation were evaluated as bad (1), good (2) and excellent (3) by surgeons, and the mean surgical satisfaction was reported as 2.4 points for both groups. In the studies performed the surgeons also stated that there was good muscle relaxation in spinal anesthesia technique, any technical problems were not encountered and the results were similar in the general anesthesia and the spinal anesthesia groups.

These results are similar to the results obtained in our study, and suggest that spinal anesthesia is a good alternative to general anesthesia for laparoscopic cholecystectomy.

One of the limitations of our study is the high intraabdominal pressure created during pneumoperitoneum. This affected hemodynamic values negatively, and contributed to the occurrence of shoulder pain. Imbelloni et al. worked under pressure of 8 mmHg, and applied intraperitoneal local anesthetic when patients felt pain. In this way, they reduced the rate of shoulder pain by 47% to 20%. However, it should be kept in mind that low pneumoperitoneum pressure may lead to limited surgical vision.

CONCLUSION

According to the results of this clinical prospective study it may be concluded that spinal anesthesia may be used as an alternative method to general anesthesia in patients undergoing laparoscopic cholecystectomy, especially when the risk of general anesthesia is too high in patients with a predetermined difficult intubation, severe respiratory disease or history of malignant hyperthermia.

REFERENCES

1. Cunningham AJ, Brull SJ. Laparoscopic cholecystectomy: anesthetic implications. Anesth Analg. 1993;76:1120-33. [CrossRef]
2. Bajwa SJ, Kulshrestha A. Anaesthesia for laparoscopic surgery: General vs regional anaesthesia. J Minim Access Surg. 2016;12:4-9. [CrossRef]
3. Kalaivani V, Vinayak SP, Sreevathsa MR, Bharati VH, Bevinaguddal Y. Laparoscopic cholecystectomy under spinal anaesthesia vs. general anaesthesia: A prospective randomised study. J Clin Diagn Res. 2014;8(8):NC01-4. [CrossRef]
4. Turkistani A, Ibraheem O, Khairy G, Alseif A, Khalil N. Spinal versus general anesthesia for laparoscopic cholecystectomy: a comparative study of cost effectiveness and side effects. Anaesth Pain & Intensive Care 2009;13:9-14.
5. Yu G, Wen Q, Qiu L, Bo L, Yu J. Laparoscopic cholecystectomy under spinal anaesthesia vs. general anaesthesia: a meta-analysis of randomized controlled trials. BMC Anesthesiol. 2015;15:176. [CrossRef]
6. Wang XX, Zhou Q, Pan DB, et al. Comparison of Postoperative Events between Spinal Anaesthesia and General Anaesthesia in Laparoscopic Cholecystectomy: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Biomed Res Int. 2016;2016:9480539. [CrossRef]
7. Ciofolo MJ, Clergue F, Seebacher J, Lefebvre G, Viars P. Ventilatory effects of laparoscopy under epidural anaesthesia. Anesth Analg. 1990;70:357-61. [CrossRef]
8. Myles PS. Bradyarrhythmias and laparoscopy: a prospective study of heart rate changes with laparoscopy. Aust N Z J Obstet Gynaecol. 1991;31:171-3. [CrossRef]
9. Longo MA, Cavaleiro BT, de Oliveira Filho GR. Laparoscopic cholecystectomy under neuraxial anesthesia compared with general anesthesia: Systematic review and meta-analyses. J Clin Anesth. 2017;41:48-54. [CrossRef]
10. Mehta PJ, Chavda HR, Wadhwa AP, Porecha MM. Comparative analysis of spinal versus general anesthesia for laparoscopic cholecystectomy: A controlled, prospective, randomized trial. Anesth Essays Res. 2010 Jul-Dec;4(2):91-5. [CrossRef]
11. Bessa SS, Katri KM, Abdel-Salam WN, El-Kayal el-SA, Tawfik TA. Spinal versus general anesthesia for day-case laparoscopic cholecystectomy: a prospective randomized study. J Laparoendosc Adv Surg Tech A. 2012;22:550-5. [CrossRef]
12. Imbelloni LE, Fornasari M, Fialho JC, Sant’Anna R, Cordeiro JA. General anesthesia versus spinal anesthesia for laparoscopic cholecystectomy. Rev Bras Anestesiol. 2010;60:217-27. [CrossRef]
13. Tzovaras G, Fafoulakis F, Pratsas K, Georgopoulou S, Stamatiou G, Hatzitheofilou C. Spinal vs general anesthesia for laparoscopic cholecystectomy: interim analysis of a controlled randomized trial. Arch Surg. 2008;143:497-501. [CrossRef]
14. Bessa SS, El-Sayes IA, El-Saiedi MK, Abdel-Baki NA, Abdel-Maksoud MM. Laparoscopic cholecystectomy under spinal versus general anesthesia: a prospective, randomized study. J Laparoendosc Adv Surg Tech A. 2010;20:515-20. [CrossRef]
15. Kar M, Kar JK, Debnath B. Experience of laparoscopic cholecystectomy under spinal anesthesia with low-pressure pneumoperitoneum--prospective study of 300 cases. Saudi J Gastroenterol. 2011;17:203-7. [CrossRef]
16. Sinha R, Gurwara AK, Gupta SC. Laparoscopic cholecystectomy under spinal anaesthesia: a study of 3492 patients. J Laparoendosc Adv Surg Tech A. 2009;19:323-7. [CrossRef]
17. Tiwari S, Chauhan A, Chaterjee P, Alam MT. Laparoscopic cholecystectomy under spinal anaesthesia: A prospective, randomised study. J Minim Access Surg. 2013;9:65-
A. Kisa et al. Comparison of General Anesthesia with Spinal Anesthesia in Laparoscopic Cholecystectomy Operations

71. [CrossRef]
18. Imbelloni LE, Sant’anna R, Fornasari M, Fialho JC. Laparoscopic cholecystectomy under spinal anesthesia: comparative study between conventional-dose and low-dose hyperbaric bupivacaine. Local Reg Anesth. 2011;4:41-6. [CrossRef]
19. Hamad MA, El-Khattary OA. Laparoscopic cholecystectomy under spinal anesthesia with nitrous oxide pneumoperitoneum: a feasibility study. Surg Endosc. 2003;17:1426-8. [CrossRef]
20. Sarli L, Costi R, Sansebastiano G, Trivelli M, Roncoroni L. Prospective randomized trial of low-pressure pneumoperitoneum for reduction of shoulder-tip pain following laparoscopy. Br J Surg. 2000;87:1161-5. [CrossRef]
21. Kehlet H. Effect of postoperative pain treatment on outcome-current status and future strategies. Langenbecks Arch Surg. 2004;389:244-9. [CrossRef]
22. Lee IO, Kim SH, Kong MH, et al. Pain after laparoscopic cholecystectomy: the effect and timing of incisional and intraperitoneal bupivacaine. Can J Anaesth. 2001;48:545-50. [CrossRef]
23. Luchetti M, Palomba R, Sica G, Massa G, Tufano R. Effectiveness and safety of combined epidural and general anesthesia for laparoscopic cholecystectomy. Reg Anesth. 1996;21:465-9.
24. Yuksek YN, Akat AZ, Gozalan U, et al. Laparoscopic cholecystectomy under spinal anesthesia. Am J Surg. 2008;195:533-6. [CrossRef]