Research Article

Neuroendocrine and Hemodynamic Effects of General Anesthesia and Spinal Anesthesia For Minimally Invasive Lumbar Disc Surgery: A Randomized Trial

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Summary

Background: Spinal anesthesia used as an alternative to general anesthesia in lumbar spinal surgical interventions could be implemented in all elective spinal surgical operations. We compared the neuroendocrine and hemodynamic effects of general and spinal anesthesia for minimally invasive lumbar disc surgery.

Methods: Fifty-six patients classified as American Society of Anesthesiologists (ASA) I–II were included in the study. Blood was drawn at 30 min and 6 and 24 h after surgery for determination of adrenocorticotropic hormone, cortisol, and glucose levels. Hemodynamic parameters were also recorded. Furthermore, the time of first voiding, the time of first mobilization, the time of first analgesic requirement, complications, and patient satisfaction were evaluated.

Results: Significant differences were detected in cortisol values at 30 min after surgery (p=0.00). No significant differences were detected in the other blood values monitored (p>0.05). The time of first voiding and discharge time were shorter in the spinal group.

Conclusion: As a result, our results show that spinal anesthesia can be a good alternative to general anesthesia for single-level lumbar disc surgery.

Key words: Spinal anesthesia, lomber disc surgery, stress response

Minimal Invaziv Lomber Disk Cerrahisinde Spinal Anestezi ve Genel Anestezinin Nöroendokrin ve Hemodinamik Etkileri: Randomize Çalışma

Özet

Giriş: Spinal anestezi, elektif spinal cerrahi operasyonlarında genel anesteziye alternative olarak kullanılabılır. Bu çalışmada minimal invaziv lomber disk cerrahisinde spinal anestezi ve genel anestezinin nöroendokrin ve hemodinamik etkilerini karşılaştırdık.


Sonuçlar: Cerrahi sonrası 30. dakikada kortizol seviyesinde anlamlı farklılık saptandı (p=0.00). Monitörize edilen diğer kan değerlerinde farklılık saptanmadı (p>0.05). İlk idrar yapma ve taburculuk zamanı spinal anestezi grubunda daha kısaydı.

Tartışma: Sonuç olarak, bu sonuçlar tek mesafe lomber disk cerrahisi için spinal anestezi genel anesteziye iyi bir alternatif olabilir.

Anahtar Kelimeler: Spinal anestezi, lomber disk cerrahisi, stres yanıt
INTRODUCTION
If lumbar disc hernia, one of the most common causes of lumbar pain, causes significant motor loss and results in severe sciatalgia that lasts for more than 3–4 weeks, surgical intervention is recommended (23). Spinal anesthesia as an alternative to general anesthesia in lumbar spinal surgical interventions may be implemented in all elective spinal surgical operations (discectomy, laminectomy, or spinal stenosis). Compared with general anesthesia, spinal anesthesia has advantages such as decreased peri-operative blood loss, easier implementation of the prone position, fewer pressure sores, shorter post-operative complications (e.g., urinary retention, pulmonary complications, and thromboembolic complications), shorter hospital stay, and decreased medical costs (11, 24). The effects of regional and general anesthesia on the stress response due to surgery has been reported studies (13, 18, 26). Whether surgical success is affected by changing the stress response, particularly its relationship to the anesthesia method, has been the subject of many studies. Regional anesthesia methods have some advantages compared with general anesthesia, such as a decreased incidence of thromboembolic complications, decreased post-operative pulmonary function, and decreased post-operative cardiac function. A decreased duration of hospital stay and less post-operative pain are also advantages of regional anesthesia (16). We designed this prospective, randomized study to compare the neuroendocrine and hemodynamic effects of general and spinal anesthesia for minimally invasive lumbar disc surgery.

MATERIAL AND METHODS
Fifty-six patients aged 18–60 years classified as American Society of Anesthesiologists (ASA) I–II for whom disc surgery had been planned, and in whom micro-discectomy was to be implemented through minimally invasive intervention, were included in the study. Patients with a contraindication for spinal anesthesia, a body mass index greater than 35, an allergic reaction to anesthetic agents, hemorrhagic diathesis history, dysfunctions of the liver or kidney, endocrine pathology, or neurologic and psychiatric disorders were excluded from the study.

Essential assessments were carried out through a pre-operative visit 1 day before the operation, and patients were informed about the general and spinal anesthesia. Informed consent was obtained from each patient. Twenty-five milligrams of dolantin (Petidin HCl ampul®, Pharma GmbH, Austria) were administered intramuscularly to all patients as premedication 1 h prior to the operation. In the operating room, routine monitoring was initiated (non-invasive blood pressure, electrocardiography with three derivations (D II), and pulse oximetry monitoring). Demographics, drug use, and additional diseases were recorded. A 20-G intravenous catheter was inserted on the back of the hand or antecubital fossa. One milligram of midazolam (Dormicum ampul® Roche, France) was applied intravenously to all patients.

Patients were divided randomly into two groups using the envelope method. Thus, the classifications were as follows: Group S: spinal anesthesia group; Group G: general anesthesia group. Blood from each patient was collected for measurement of basal glucose, cortisol, and ACTH values. Patients in Group S were placed in the lateral decubitus position after being infused with 500 ml of 0.9% NaCl. After ensuring skin antisepsis, the local anesthetic agent was applied to the skin with prilocaine (Citanest®, Astra Zeneca, England). Fifteen milligrams of 5% hyperbaric bupivacaine (Marcaine Heavy, Astra Zeneca, England) were applied after monitoring of free cerebrospinal fluid flow by accessing through the L3–4 or L4–5 inter-vertebral spaces using a 25-G spinal needle. The patient was then placed in the supine position. When the anesthesia level reached the T 10 dermatomal level, the
The patient was placed in the prone position. Induction was achieved through administration of 5 mg/kg thiopental sodium (Pental Sodium®, I.E Ulagay, Turkey) 0.1 mg/kg vecuronium bromide (Norcuron®, Schering-Plough USA), and 1 µg/kg intravenous fentanyl (Fentanyl®, Janssen-Cilag, Belgium) in Group G. Anesthesia was maintained using 4–5% desflurane (Suprane®, Baxter, USA), 50% O₂ and 50% N₂O after intubation. Next, the patient was placed in the prone position, and then 1 µg/kg remifentanil (Ultiva®, Glaxo Smith Kline, Italy) was administered according to the hemodynamic response. Blood was drawn at 30 min, and 6 and 24 h after surgery for the measurement of ACTH, cortisol, and glucose levels. Hemodynamic parameters were recorded, as was the time of first voiding, time of first mobilization, first analgesia requirement, complications (headache, urinary retention, neurological complications, nausea, and vomiting), and patient satisfaction.

**Statistical analysis**

A t-test was used to evaluate the difference between the independent groups regarding age, body weight, height, and surgical duration. A chi-squared test was used to assess the differences between the groups in terms of ASA classification, diabetes mellitus status, hypertension, presence of additional chronic diseases, applied spinal space, smoking status, and whether an opioid was applied. The Greenhouse-Geisser test was used to compare the heart rate, as well as the systolic, diastolic, and average blood pressure values between the repetitions; a t-test was used to evaluate differences between the independent groups. Additionally, a t-test was used to evaluate plasma cortisol levels. ACTH and glucose values were analyzed using independent tests. The SPSS version 11.5 statistical software for Windows XP was used for statistical analyses, and a p value less than 0.05 was deemed to indicate statistical significance.

**RESULTS**

There was no difference between the groups in terms of height, weight, or age (p=0.751, 0.256, and 0.053, respectively). Surgical duration was shorter in the spinal group (p=0.01). Although more patients were included in the ASA I group (p=0.012), no difference was detected in terms of gender distribution between the groups (p=0.593).

The basal heart rate was monitored before and after anesthesia, at the beginning of surgery, during the surgery at 5-min intervals, and at the completion of the surgery. Postoperatively, monitoring was performed during the initial 30 min, and at 6 and 24 h.

The basal heart rate among repetitions did not differ significantly within either group during the intra-operative period (p>0.05). There was no significant difference among the repeated systolic blood pressure measurements in the spinal anesthesia (p>0.05) or general anesthesia (p>0.05) group. No significant difference was found among the diastolic blood pressure measurements in the spinal anesthesia group (p>0.05) or general anesthesia (p>0.05) group. There was no statistically significant difference in the diastolic blood pressure between the groups at 5 min and at the end of anesthesia (p=0.002 and p=0.000, respectively).

There was no significant difference among the repeated average blood pressure measurements in the spinal anesthesia (p>0.05) or general anesthesia (p>0.05) group. There was no significant difference in average blood pressure between the groups at 5 min or at the completion of surgery (p=0.007 and p=0.000, respectively).

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The neuroendocrine response and blood glucose, ACTH, and cortisol levels were evaluated at 30 min, and 6 and 24 h after the surgery (Table 1). Blood glucose levels at 30 min, and 6 and 24 h after surgery did not differ significantly between the two groups (p>0.05) (Figure 1).
No significant difference in ACTH values, as an indicator of the stress response, was detected between the groups (p>0.05) (Figure 2). A significant difference between the two groups was found in cortisol values at 30 min after surgery (p=0.00). No significant difference was detected in other parameters being monitored. (p>0.05) (Figure 3). The patients were monitored for 24 h after the operation for complications such as headache, nausea/vomiting, and urinary retention. Rates of most complication were similar; however, nausea/vomiting was more common in the general anesthesia group. Urinary retention occurred in one patient in the spinal anesthesia group, but none in the general anesthesia group (Table 2). The patient satisfaction rates were 92.9% and 89.3% in the spinal and general anesthesia groups, respectively. The times of first voiding, first mobilization, first analgesic requirement, and discharge during the 24 h following surgery were reported. The times of first voiding and discharge were shorter in the spinal group, whereas the other parameters differed between the two groups (Table 3).

Table 1. Neuroendocrine hormones (Average ± SD)

<table>
<thead>
<tr>
<th></th>
<th>Group S (group with spinal anesthesia)</th>
<th>Group G (group with general anesthesia)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basal glucose (mg/dl)</td>
<td>108.6 ± 21.3</td>
<td>103.8 ± 23.8</td>
</tr>
<tr>
<td>30th minute glucose</td>
<td>114.9 ± 22.8</td>
<td>112.2 ± 26.2</td>
</tr>
<tr>
<td>6th hour glucose</td>
<td>111.9 ± 36.7</td>
<td>101.1 ± 17.8</td>
</tr>
<tr>
<td>24th hour glucose</td>
<td>129.2 ± 32.8</td>
<td>126.3 ± 35.1</td>
</tr>
<tr>
<td>Basal ACTH (pg/ml)</td>
<td>24.5 ± 28.5</td>
<td>58.9 ± 152</td>
</tr>
<tr>
<td>30th minute ACTH</td>
<td>58.1 ± 62.2</td>
<td>59.7 ± 203</td>
</tr>
<tr>
<td>6th hour ACTH</td>
<td>14.5 ± 17.7</td>
<td>52.5 ± 163.7</td>
</tr>
<tr>
<td>24th hour ACTH</td>
<td>37.4 ± 107.5</td>
<td>39.3 ± 140.3</td>
</tr>
<tr>
<td>Basal cortisol (µ/dl)</td>
<td>17.4 ± 7.7</td>
<td>16.4 ± 6.5</td>
</tr>
<tr>
<td>30th minute cortisol</td>
<td>21.2 ± 8.2</td>
<td>12.4 ± 6.8</td>
</tr>
<tr>
<td>6th hour cortisol</td>
<td>10.5 ± 8</td>
<td>14.4 ± 10.1</td>
</tr>
<tr>
<td>24th hour cortisol</td>
<td>19.3 ± 22.2</td>
<td>17.4 ± 10.2</td>
</tr>
</tbody>
</table>
Figure 1: Plasma glucose level changes (mg/dl).

Figure 2: Plasma ACTH level changes (pg/ml)

Figure 3: Plasma cortisol level changes (µ/dl)
Table 2. Postoperative complications (as number and percentage)

<table>
<thead>
<tr>
<th></th>
<th>Group SA (group with spinal anesthesia)</th>
<th>Group GA (group with general anesthesia)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>14,3 %</td>
<td>10,7 %</td>
</tr>
<tr>
<td>Nausea-vomiting</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>Urinary retention</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>3,7 %</td>
<td>0 %</td>
</tr>
</tbody>
</table>

Table 3. Other parameters monitored (Average ± SD) (As hour)

<table>
<thead>
<tr>
<th></th>
<th>Group SA (group with spinal anesthesia)</th>
<th>Group GA (group with general anesthesia)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time of first voiding</td>
<td>7,14 ± 1,8</td>
<td>9,6 ± 2,8</td>
</tr>
<tr>
<td>Time of first mobilization</td>
<td>8,1 ± 2,5</td>
<td>9,1 ± 1,9</td>
</tr>
<tr>
<td>First analgesic requirement time</td>
<td>10,2 ± 2,7</td>
<td>10,4 ± 7,2</td>
</tr>
<tr>
<td>Discharge time</td>
<td>22,3 ± 3,4</td>
<td>29,7 ± 9,7</td>
</tr>
</tbody>
</table>

DISCUSSION

Spinal anesthesia use for spinal surgery has become increasingly widespread. Particularly, the positioning of the patient helps to prevent complications, such as nerve injury, suffered in the prone position during general anesthesia. Among other advantages are less blood loss and fewer thromboembolic complications compared with general anesthesia. In addition, complications such as nausea/vomiting and urinary retention are found to occur less frequently in spinal anesthesia. These advantages lead to increased patient satisfaction and decreased duration of hospital stay (11,12,24). Patients with spinal anesthesia, when they awake, may be uncomfortable because of lying in the same position for a long period. General anesthesia is usually preferred for patients who have a greater probability of more blood loss and whose surgery will be of a duration longer than 2 h. General anesthesia is also preferred for obese patients due to technical difficulties. In the prone position, the pressure of the abdominal organs on the diaphragm may lead to a decrease in the lung capacity, causing decreased lung compliance in a spontaneously ventilating patient and an increased respiratory rate (9).
Both spinal and general anesthesia may lead to hypotension during surgery in the prone position. Poon et al. found that hypotension occurs while in the prone position due to a decrease in the cardiac index and stroke volume. In the prospective randomized study by Jellish et al., blood pressure and heart rate were lower during spinal surgery with spinal anesthesia compared to general anesthesia. In the retrospective study by Tetzlaff et al., 803 patients were monitored, and spinal anaesthesia was shown to cause a greater decrease in blood pressure and heart rate compared with general anesthesia. Becq et al. reported better preoperative hemodynamic stability with spinal anesthesia. Tetzlaff et al. reported that the variability in the heart rate was less with spinal anaesthesia than with general anaesthesia. In the present study, a significant difference was found in the heart rate monitors between the two groups only following spinal anesthesia and intubation; no significant difference was found in the other spaces monitored. Systolic blood pressure did not differ between the two groups, whereas diastolic blood pressure was lower in the spinal group post-application and at 5 min after surgery. The average blood pressure was lower in the spinal group post-application. This may be due to the fluid replacement performed at the pre-spinal stage.

More nausea/vomiting occurred with general anesthesia, likely due to use of N2O. The effects of general anesthesia on gastric leverage are one of the factors that increase the nausea/vomiting rate. Less nausea/vomiting occurs with spinal anesthesia. Jellish et al., Tetzlaff et al., and McLain et al. reported that nausea/vomiting was significantly less frequent with spinal anesthesia. In the prospective study by Demirel et al., nausea/vomiting was more frequent in the general anesthesia group. In the present study, no postoperative nausea/vomiting was observed in the spinal group, whereas it was detected in four patients in the general anesthesia group. In many studies of spinal anesthesia, acute pain scores were reported to be low. Two mechanisms were regarded as being responsible: spinal anesthesia inhibiting nociceptive pathways and sensorial blockade disappearing later than motor blockade. In the spinal anesthesia studies by Jellish et al., Tetzlaff et al., McLain et al., the postoperative pain score was lower in the spinal anesthesia group. In the present study, the prospective pain score was lower in the general anesthesia group, albeit not significantly so. This may be due to selection of a patient group undergoing invasive surgery. Additionally, intraoperative administration of opioids may have influenced pain scores. Post-spinal-anesthesia urinary retention is a frequent complication that results from relaxation of the bladder muscular tonus. Urinary retention occurs frequently in spinal anesthesia with intrathecal opioid use. Jellish et al. and Tetzlaff et al., reported that urinary retention was similar in the spinal and general anesthesia groups. McLain found that urinary retention was more common in the general anesthesia group. In the study by Young et al. of inguinal hernias, more urinary retention was detected in the general anesthesia group. In the spinal study by Silver et al., less urinary retention was detected in the spinal anesthesia group. In the present study, the time of first voiding was shorter in the spinal group; likely due to non-use of intrathecal opioids. Motor blockade due to spinal anesthesia was speculated to be responsible for delaying mobilization when spinal and general anesthesia were compared. The time of first mobilization was similar between the two groups.

Another possible complication of spinal anesthesia is headache. In the spinal studies by the Jellish, Tetzlaff, and McLain groups, a lower incidence of headache was detected according to the general anesthesia.
Spinal anesthesia is associated with a shorter hospital stay compared with general anesthesia. In the study of arthroscopy by Parness et al., the hospital stay durations of the spinal and general anesthesia groups were similar; however, this was considered to be dependent on the propofol used in general anesthesia. Likewise, in the present study, the hospital stay duration of the spinal anesthesia group was significantly shorter than that of the general anesthesia group.

One of the most important developments in recent years is the elucidation of the physiological variables arising in anesthesia and surgery. The stress response during the post-surgical period can be altered and its magnitude depends on the type of surgery. Catecholamine and cortisol secretion from the adrenal gland and ACTH secretion from the pituitary gland increase due to afferent signals from the surgical area. Various surgical impulses cause various hormone responses. When cortisol, ACTH, epinephrine, and norepinephrine levels were examined, increased catabolism results under surgical stimulus. Catecholamine secretion from the adrenal medulla and norepinephrine secretion from pre-synaptic nerve endings increase as a result of hypothalamic activation of the sympathetic system. Increased sympathetic activation leads to tachycardia and hypertension. Additionally, in particular, the liver, kidney, and pancreas, and some other visceral organs are affected.

ACTH stimulates adrenal secretion of glucocorticoids; thus, the cortisol concentration in the circulation increases. A surgical impulse is one of the most potent activators of ACTH and cortisol secretion. Levels of these hormones begin to increase when surgery begins. Cortisol levels increase due to ACTH stimulation at the start of surgery. They may increase by as much as fourfold during the first 4–6 h, depending on the extent of the surgery. The cortisol response may change according to the anesthetic approach. Increased cortisol generally inhibits ACTH secretion. However, this mechanism fails after surgery, and hormone values remain high. Cortisol has a complex metabolic effect on carbohydrate, protein, and fat metabolism, causing gluconeogenesis and protein destruction in the liver. Glucose use by the cells is blocked; thus, blood sugar levels increase. The insulin concentration may decrease during anesthesia induction and surgery due to α-adrenergic inhibition of β-cell secretion. In addition, the cellular response against insulin fails during the preoperative period. There is an increase in the plasma glucagon concentration post-surgery, but this does not contribute to the hyperglycemic response.

General anesthesia limits the response to surgery; however, even deep anesthesia cannot abrogate it completely. Volatile anesthetics have a minimal effect on endocrine and metabolic functions. It has long been known that opioids suppress hypothalamic and pituitary hormone secretion. Neural blockage because of regional anesthesia with local anesthetic agents has a direct effect on endocrine and metabolic responses. The main mechanism here is prevention of nociceptive signals from the surgical area from reaching the central nervous system. This inhibitor effect involves both afferent and efferent pathways; however, it differs for the endocrine glands. Although secretion of pituitary hormones involves afferent pathways, adrenocortical hormone secretion is more complex. Neural blockage from T4 to S5 suppresses the cortisol response. The hyperglycemic response to surgery depends on the secretion of stress hormones, which is mediated by afferent and efferent neural pathways.

Poon et al. achieved better stress response control by adding epidural anesthesia to general anesthesia. Opioids have been shown to suppress the stress response. In a study of lower abdominal surgery, growth hormone, cortisol, and glucose with 50
µg/kg fentanyl suppressed the stress response. However, systemic opioids may be insufficient to suppress the response to upper abdominal surgeries. In one study of cholecystectomies using 100 µg/kg fentanyl, the stress response was suppressed; however, patients also required postoperative ventilation\(^{(8)}\).

Most studies of neural blocks are related to epidural anesthesia, and few have addressed spinal anesthesia and stress. In a study of hysterectomies, cortisol and glucose responses were suppressed by epidural blockage between T4 and S4\(^{(8)}\).

Moller compared stress responses following spinal and general anesthesia in abdominal hysterectomies, and reported that spinal anesthesia had a temporary inhibitory effect, which was associated with the sensorial block level\(^{(18)}\).

In the general anesthesia group, although the hyperglycemic response was suppressed at the 6 min, the blood sugar level was high at 30 min and 24 h. In the spinal anesthesia group, hyperglycemia was identified in the spaces monitored; spinal anesthesia did not suppress this response. However, there was no significant difference between the two groups; additionally, the blood sugar levels were not excessive. In the spinal anesthesia group, the stress response (in terms of ACTH levels) was suppressed beginning at 6 min; however, in the general anesthesia group, it was suppressed at 24 h, as indicated by normalization of ACTH values. There was no significant difference between the two groups. The cortisol level was high at only 30 min, whereas it was normal in both groups at the other time points. Thus, the stress response was suppressed. Suppression of the stress response did not differ significantly between the groups. In stress response-based studies, epidural anesthesia is preferred over spinal anesthesia for central blocks\(^{(21,26)}\). The selected patients had generally undergone major operations, such as abdominal or thigh surgery. However, the surgical intervention used in this study was microdiscectomy, a minimally invasive technique. The stress response may be considered to be minor compared with major interventions due to use of a small incision. Thus, the stress response was suppressed effectively in all patients in this study.

Therefore, spinal anesthesia is a good alternative to general anesthesia for single-level lumbar disc surgery.

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