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SCIENTIFIC ARTICLE

The comparison of levobupivacaine in continuous or single dose spinal anesthesia for transurethral resection of prostate surgery

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Abstract
Background: The aim of the study is to compare the efficacy of levobupivacaine induced continuous spinal anesthesia (CSA) versus single dose spinal anesthesia (SDSA) in patients who are planned to undergo transurethral prostate resection.
Methods: Sixty years or older, ASA I–II or III, 50 patients were included in the study. 12.5 mg 0.5% levobupivacaine were administered intrathecally in SDSA group. In CSA group, initially 2 mL of 0.25% levobupivacaine were administered through spinal catheter. In order to achieve sensory block level at T10 dermatome, additional 1 mL of 0.25% levobupivacaine were administered through the catheter in every 10 min. Hemodynamic parameters and block characteristics were recorded. Preoperative and postoperative blood samples of the patients were drawn to determine plasma cortisone and plasma epinephrine levels.
Results: CSA technique provided better hemodynamic stability compared to SDSA technique particularly 90 min after intrathecal administration. The rise in sensory block level was rapid and the time to reach surgical anesthesia was shorter in SDSA group. Motor block developed faster in SDSA group. In CSA group, similar anesthesia level was achieved by using lower levobupivacaine dose and which was related to faster recovery. Although, both techniques were effective in preventing surgical stress respond, postoperative cortisone levels were suppressed more in SDSA group.

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Conclusion: CSA technique with 0.25% levobupivacaine can be used as a regional anesthesia method for elderly patients planned to have TUR-P operation.

Introduction

Anesthesia is applied in 10–20% of urologic interventions. Anesthetic methods chosen within general principles are topical, regional and general.[1,2] Most patients with bladder obstruction caused by benign prostatic hyperplasia are successfully treated by transurethral resection of the prostate (TUR-P).[3] TUR-P is often performed on older patients with impaired renal function, cardiovascular and respiratory problems. Research has found many side effects of TUR-P including bleeding, transurethral resection syndrome (TUR), bladder perforation, hypothermia, intraoperative and early postoperative occurrence of disseminated intravascular coagulation, with high reported morbidity rates. To minimize hemodynamic changes in these patients it is important to provide stable anesthesia. General anesthesia may make identification of complications such as TUR syndrome and bladder perforation difficult, so regional anesthesia is the preferred method in suitable TUR-P cases.[4–7]

Single-dose spinal anesthesia (SDSA) is widely used in these interventions though it has the disadvantage of not providing the required duration in operations that run longer than expected. With the continuous spinal anesthesia (CSA) technique, local anesthetic dose can repeated, thus making it possible to use this spinal anesthesia method in operations with long duration.[8–12] Another advantage of CSA is that it enables to titrate the dose of local anesthetic thus allowing better control of sensory and motor block level, no risk of local anesthetic toxicity and providing shorter recovery periods. Compared to SDSA, its most important advantage is that it provides perfect hemodynamic stability. Furthermore, spinal catheter may be inserted in regional anesthesia preparation room before the operation, thus preventing loss of time between operations.[10,13,14]

Levobupivacaine, a bupivacaine S isomer commonly used in spinal anesthesia (SA), has less side effects on the cardiovascular (CVS) and central nervous systems (CNS) than bupivacaine with similar effective onset time and duration.[7,15–17] Although levobupivacaine use in various regional anesthesia techniques have been reported previously, description of its use in CSA is limited. We have hypothesized that levobupivacaine provides better hemodynamic stability when used in CSA compared to SDSA. In order to test this hypothesis, patients scheduled to have TUR-P operation were administered either SDSA or CSA with levobupivacaine; hemodynamics, sensory-motor block levels, anesthetic quality and complications were compared.

Materials and methods

After receiving permission from Bulent Ecevit University Medical Faculty Hospital Ethics Committee (06.12.2007, Decision no. 2007/09/17), this research was carried out in the Department of Anesthesiology and Reanimation between December 2007 and June 2008. Fifty patients over the age of 60 scheduled to have elective TUR-P interventions at ASA I–III risk groups were included in the study after reading the informed consent form. The patients were randomized into either continuous spinal anesthesia group (Group CSA, n:25) or single-dose spinal anesthesia group (Group SDSA, n:25) by randomized numbers table.

Exclusion criteria were refusing to be included in the study, allergies to the research drugs, severe cardiac failure (unstable coronary artery disease, 2nd and 3rd degree heart block, congestive heart failure, ventricular tachyarrhythmia) and valvular heart disease (serious aortic stenosis), coagulation abnormalities, low molecular weight heparin administration in the previous 12 h, intake of non-steroidal anti-inflammatory drug within the 24 h, history of alcohol or drug addiction, presence of neurologic disorders or psychiatric disease.

All the patients were premedicated with 0.03 mg/kg midozolam (Dormicum®) intramuscularly 30 min prior to their arrival to operation theater. Patients were taken to the preoperative preparation unit and were monitored (non-invasive blood pressure, heart rate and peripheral oxygen saturation while breathing room air) these values were recorded as control values. Patients were given 4 l/min oxygen through a mask, a 20 G cannula was inserted for intravenous access and 10 mL/kg 0.09% saline was infused within 30 min, afterwards the rate was set at 5 mL kg/h. Blood samples taken from each patient while opening the vein was centrifuged to separated plasma from serum and stored in a freezer at −20 °C.

All patients had lumbar puncture under aseptic conditions, while sitting, between L3–4 or L 2–3 according to anesthesist's preference. The lumbar puncture level was recorded. Skin and subcutaneous 2 mL 2% lidocaine (Aritmal® 5 mL ampoule) infiltration anesthesia was given with a 22 G needle. Anesthesia was begun for Group CSA with 2 mL 0.25% levobupivacaine after a 22 G spinal catheter (Spinocath®) was placed 2–3 cm into the intrathecal interval. After the 10th min if the level of sensory block had not reached T10, an extra 1 mL 0.25% levobupivacaine was given through the catheter, this was repeated at 10 min intervals until T10 block level was reached. The total dose of levobupivacaine was recorded.

Spinal anesthesia was induced in group SDSA patients with 12.5 mg (2.5 mL) 0.5% levobupivacaine injected into the intrathecal interval with a 22 G Quinke needle.

After the injection blood pressure, heart rate, SpO₂, pinprick test for sensory block level, and modified Bromage scale (MBS) were used to evaluate degree of motor block every 2.5 min up to the 15th min and every 5 min between

15 and 45 min. (MBS: 0 no paralysis, patient can fully flex foot and knee; 1 Can only move knee and foot, cannot lift straight leg; 2 cannot bend knee, can only move foot; 3 full paralysis.) After 45 min the patients were taken to the operating room.

In both groups the time from the injection to sensory block level reaching dermatome T10 was recorded as the surgical anesthetic duration. It was planned that patients who reached dermatome T10 and above sensory block level gave permission for the operation. After spinal injection until MBS 1 was reached was denoted the motor block initiation time. From the injection to peak dermatome that is sensory block level reached maximum dermatome, was called the peak dermatome time. From the start of the surgical procedure to the end was the operation duration.

Sensory block level was checked using the pin-prick test (needle prick). Sensory block level was assumed to have reached the dermatome when the patient no longer felt the needle prick.

When mean arterial blood pressure (MAP) decreased 20% from the basal level hypotension was diagnosed and 5 mg ephedrine HCL (Osel drugs) was administered. Heart rate below 50 beats per min was accepted as bradycardia and 0.5 mg atropine (atropine 1 mL amp, Drogsan) was administered. Total liquids given to the patient, as well as ephedrine and atropine doses were recorded.

Patients taken to the operating theater were monitored using an ADU anesthetic monitor (Datex-Ohmeda® S/5 Anesthetic Monitor) for 5-lead surface electrocardiogram (ECG, DII), SpO$_2$ and non-invasive arterial blood pressure.

After the operation finished the CSA group had the catheter removed. Both groups were given a PCA unit (Abbot Pain Management Provider) with iv morphine (bolus dose: 2 mg, lock-out time 30 min) for postoperative analgesia. From intrathecal injection to first use of the PCA was recorded as the first analgesic duration.

Following intrathecal injection all patients were monitored at 50, 60, 70, 80, 90, 100, 110, 120, 150, 180 min and 4, 6, 9, 12, 15, 18 and 24 h. Values for blood pressure, heart rate, SpO$_2$, VRS (verbal pain evaluation scoring), sensory block level, MBS score, PCA machine requests (Dem), number of times drugs were administered by PCA (Del) and total morphine given by PCA were recorded.

Degree of pain was evaluated using VRS (0: no pain; 1 slight pain; 2 moderate pain; 3 severe pain; 4 very severe pain; 5 unbearable pain). From peak dermatome sensory block until it regressed two levels was recorded as the second dermatome reduction duration. From spinal injection to MBS score of 0 was recorded as Bromage scale 0 duration. Eight hours after the operation blood samples from all patients were centrifuged to separate serum from plasma and stored in a freezer at −20 °C. At the end of the research serum cortisol and plasma adrenaline levels in preoperative and postoperative blood samples were measured using the ELISA method.

Statistical analysis

SPSS 11.5 program was used for statistical analysis of data. The data was analyzed for normal distribution using the

Table 1 Demographic data (mean ± SD).

Group	Group CSA (n = 25)	Group SDSA (n = 25)	p
Age (year)	71.04 ± 6.62	70.68 ± 5.68	0.838
Weight (kg)	79.6 ± 11.39	80.24 ± 11.06	0.841
Operation time (min)	50.00 ± 7.79	51.44 ± 8.78	0.543
ASA (I/II/III)	3/13/9	2/15/8	0.818

Kolmogorov Smirnoff test. The Mann Whitney U test was used to compare the following continuous data from the two groups: operation duration, height, weight, age, blood pressure, heart rate, sensory block level, highest sensory block level, sensory block dermatome T10 time, sensory block two segment regression time, MBS, VRS, time of first analgesic dose, total analgesic use, PCA requests and number of times drugs were administered by PCA Del/Dem values, total atropine and ephedrine use, and cortisol and adrenalin levels. To analyze the repetition of these data within the groups the Wilcoxon test was used. The chi-square test was used to analyze frequency (%) results of ASA physical classification, lumbar puncture level, nausea-vomiting and side effects. Descriptive statistics for the data such as mean and standard deviation (mean ± SD), mode and frequency (number and %) were determined. Graphs of the changes in difference between the groups against time were constructed. A value of $p < 0.05$ was accepted as significant.

Results

The study comprised a total of 50 patients in 2 groups, all patients completed the protocol.

Demographic data

There were no statistically significant differences between the two groups in terms of age, body weight, height, ASA risk class and operation duration (Table 1).

Hemodynamic changes

Comparing the groups blood pressure in the 90, 100, 120, 150, 180 min and 4, 6, 9, 12, 15, 18 and 24 h after intrathecal injection the CSA group was significantly higher than the SDSA group ($p < 0.05$) (Fig. 1).

Within the CSA group blood pressure in the 2.5, 5, 7.5, 10, 12.5, 15, 20, 25 and 30 min after intrathecal injection was significantly lower than the control values ($p < 0.05$) (Fig. 1).

Within the SDSA group when blood pressure changes were examined they were found to be significantly lower than the control values at all times ($p < 0.05$) (Fig. 1).

There was no statistical difference between heart rate in the two groups at any measurement time ($p > 0.05$) (Fig. 2).

Within each group heart rate was significantly lower than control values at all times after intrathecal injection ($p < 0.05$) (Fig. 2).
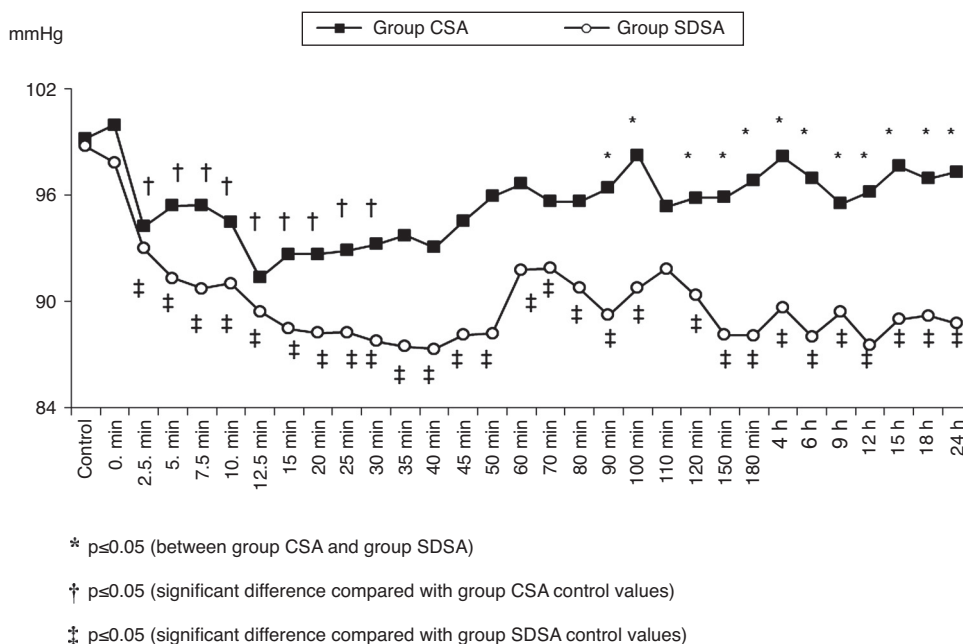
* p≤0.05 (between group CSA and group SDSA)

† p≤0.05 (significant difference compared with group CSA control values)

‡ p≤0.05 (significant difference compared with group SDSA control values)

Figure 1   Changes in mean arterial blood pressure (MAP). *$p < 0.05$ (between Group CSA and Group SDSA). †$p < 0.05$ (significant difference compared with Group CSA control values). ‡$p < 0.05$ (significant difference compared with Group SDSA control values).
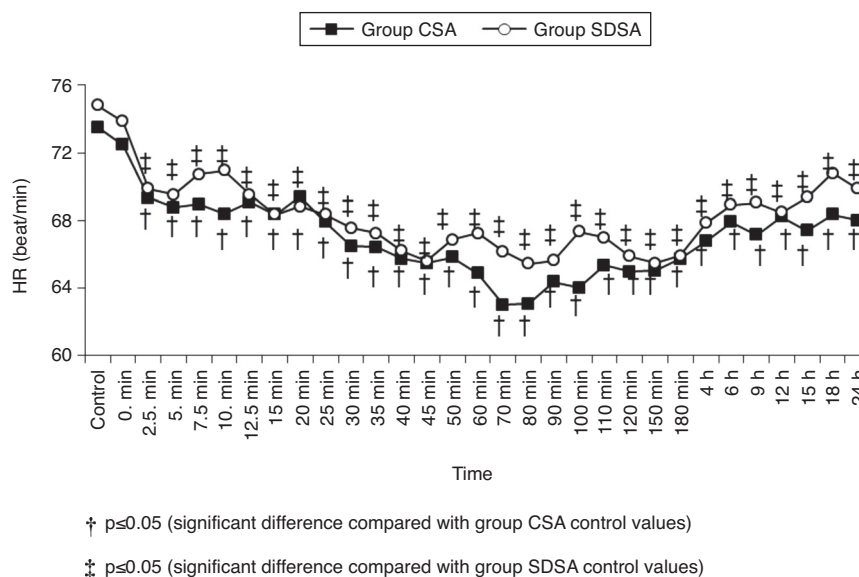

† p≤0.05 (significant difference compared with group CSA control values)

‡ p≤0.05 (significant difference compared with group SDSA control values)

Figure 2   Changes in heart rate (HR). †$p < 0.05$ (significant difference compared with Group CSA control values). ‡$p < 0.05$ (significant difference compared with Group SDSA control values).

Anesthetic properties

Lumbar puncture was performed at L2–L3 interval in 8 and at L3–L4 interval in 17 patients in the CSA group; 6 patients had lumbar puncture at L2–L3 interval and 19 patients at L3–L4 interval in the SDSA group. There was no statistically significant difference in lumbar puncture level between the two groups ($p > 0.05$).

Comparing the groups modified Bromage scores (MBS) from 5 to 120 min values were significantly higher in group SDSA than in group CSA ($p < 0.05$) (Fig. 3).

Comparing the groups sensory block levels at 2.5, 5, 7.5, 10, 12.5, 15, 20, 25, 30 and 35 min after intrathecal injection the SDSA group values were significantly higher than the CSA group ($p > 0.05$) (Fig. 4).

No statistically significant difference was found between VRS scores for the groups ($p > 0.05$). Average peak dermatome values were T8 for the CSA group and T7 for the SDSA group. There was no significant difference between the two groups peak dermatome values ($p > 0.05$).

Comparing the groups block times average peak duration, surgical anesthetic duration, and motor block start
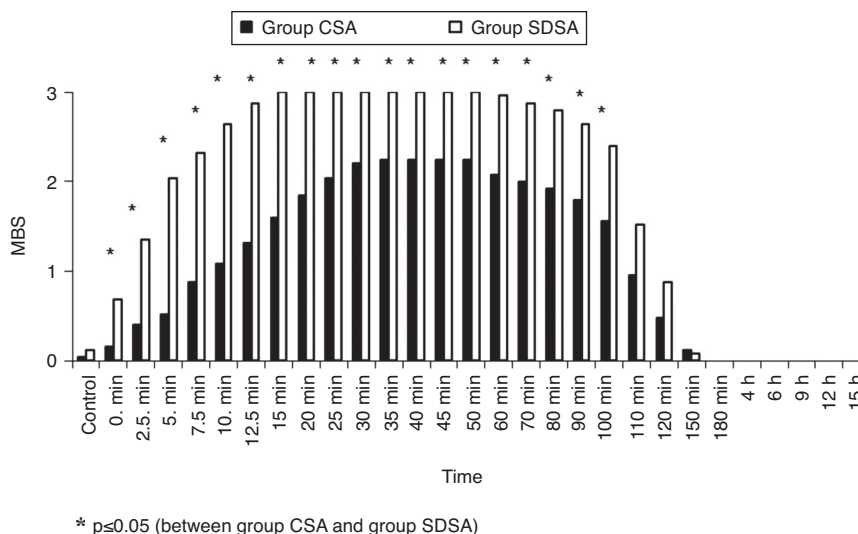
Figure 3 MBS changes in the groups. *$p < 0.05$ (between Group CSA and Group SDSA).

Table 2 Block Times (min) (mean ± SD).

Block times	Group CSA ($n = 25$)	Group SDSA ($n = 25$)	p
Time to reach peak dermatome	31.64 ± 11.94	25.10 ± 5.89	0.019*
Two segment regression time	79.28 ± 18.66	90.08 ± 14.66	0.030*
Surgical operation time	18.56 ± 6.31	13.08 ± 4.34	0.010*
Motor block start time	13.04 ± 7.10	6.04 ± 2.30	0.000*
Time to reach MBS 0	170.28 ± 51.32	186.04 ± 35.13	0.211
First analgesic time	268.88 ± 94.52	253.60 ± 92.46	0.566

* $p < 0.05$ (between Group CSA and Group SDSA).

time in the SDSA group was significantly shorter than in the CSA group. At the same time the two segment regression time was significantly longer in group SDSA than in group CSA ($p < 0.05$) (Table 2). No significant difference was found between the two groups MBS 0 and first use of analgesia times ($p > 0.05$) (Table 2).

Group SDSA used a significantly higher dose of levobupivacaine than group CSA ($p < 0.05$). There was no statistically
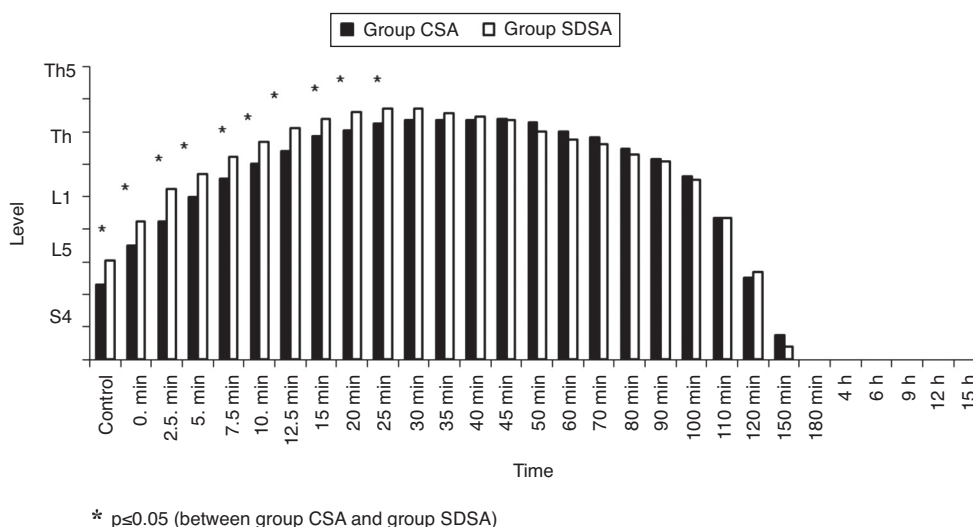

Figure 4 Sensory level changes in the groups. *$p < 0.05$ (between Group CSA and Group SDSA).

Table 3 Total drugs and liquids given (mean ± SD).

| Totals	Group CSA (n = 25)	Group SDSA (n = 25)	p
Total levobupivacaine	8.70 ± 1.63	12.50 ± 0.00	0.000[*]
Total morphine	8.00 ± 3.78	6.96 ± 2.83	0.278
Total ephedrine	0.20 ± 1.00	1.20 ± 3.31	0.160
Total atropine	0.02 ± 0.1	0.04 ± 0.13	0.561
Total liquids	1290.20 ± 180.01	1337.60 ± 148.86	0.315

[*] $p < 0.05$ (between Group CSA and Group SDSA).

Table 4 Preoperative and postoperative adrenalin and cortisol levels (mean ± SD).

Group	Group CSA (n = 22)	Group SDSA (n = 22)	p
Preop Adrenalin	249.90 ± 62.63	265.40 ± 70.90	0.446
Postop Adrenalin	190.04 ± 52.63[†]	180.76 ± 54.77[‡]	0.570
Preop Cortisol	168.95 ± 85.51	134.22 ± 51.07	0.111
Postop Cortisol	127.51 ± 57.10[†]	89.37 ± 32.98[‡,*]	0.010

[*] $p < 0.05$ (between Group CSA and Group SDSA).
[†] $p < 0.05$ (significant difference compared with Group CSA control values).
[‡] $p < 0.05$ (significant difference compared with Group SDSA control values).
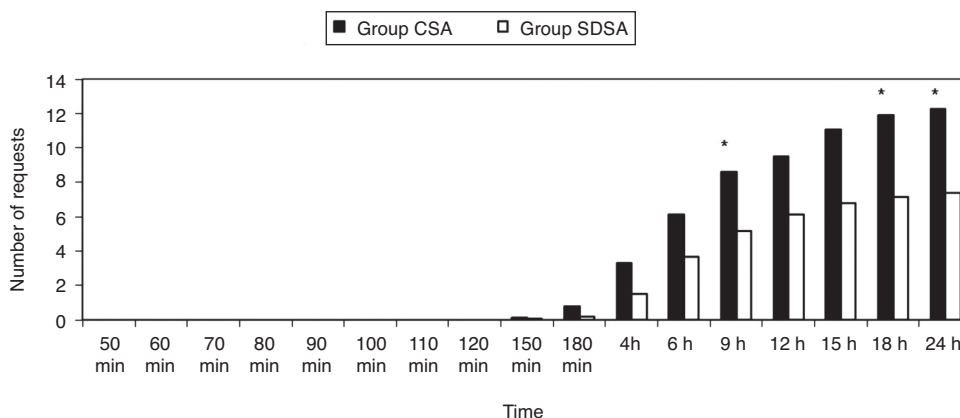
* p≤0.05 (between group CSA and group SDSA)

Figure 5 Average number of requests from the PCA unit. *$p < 0.05$ (between Group CSA and Group SDSA).

significant difference between the two groups average consumption of morphine, ephedrine, atropine and liquids ($p > 0.05$) (Table 3).

No difference was found in the number of doses given by the two groups PCA machines ($p > 0.05$). Comparing the number of requests to the PCA machines at 9, 18 and 24 h the CSA group requests were significantly higher than the SDSA group ($p < 0.05$) (Fig. 5).

No significant difference was found between the two groups plasma adrenaline levels ($p > 0.05$) (Table 4).

Within each group postoperative plasma adrenalin levels were significantly lower than the preoperative control levels ($p < 0.05$) (Table 4).

Comparing the groups' postoperative serum cortisol levels, the SDSA group levels were significantly lower than the CSA group levels ($p < 0.05$) (Table 4).

Within both groups postoperative serum cortisol levels were significantly lower than preoperative control levels ($p < 0.05$) (Table 4).

Comparing side effects in both groups, while there was no difference between the groups in terms of nausea, vomiting, respiratory depression, headache and rash, lower back pain in group CSA was significantly greater than in group SDSA ($p < 0.05$) (Table 5).

Table 5 Side effects (n, %).

Group	Group CSA (n = 25)	Group SDSA (n = 25)	p
Nausea:	0	2 (8%)	0.153
Vomiting:	0	0	1.000
Respiratory depression:	0	0	1.000
Headache:	0	1 (4%)	0.317
Lower back pain:	9 (36%)	2 (8%)	0.018[*]
Rash:	0	0	1.000

[*] $p < 0.05$ (between Group CSA and Group SDSA).

Discussion

This study compared continuous spinal anesthesia with single-dose spinal anesthesia using levobupivacaine in geriatric patients undergoing transurethral urologic interventions. We found that continuous spinal anesthesia provided better hemodynamic stability, shorter recovery periods and equal anesthetic quality.

In older patients increases in health problems combined with suppressed physiologic compensatory mechanisms means that hemodynamic instability linked to spinal anesthesia may be more serious and last longer. Rapid spread of sympathetic block in spinal anesthesia may cause an increase in morbidity, especially in older patients with reduced cardiovascular adaptation mechanisms.[18] One of the most important factors to be aware of in patients of increased age and with accompanying diseases is hemodynamic stability. In a prospective study on cardiac arrest linked to anesthesia Biboulet et al.[19] determined the most important factors in cardiac arrest in patients over 84 and with an ASA risk factor of 3 and above. They found inappropriate anesthetic doses, hypovolemia and hypoxia due to difficulty keeping the airway open were the most common reasons for cardiac arrest. Especially in patients who are older, or have cardiovascular and respiratory system problems, even low doses may result in greater anesthetic levels, so techniques such as CSA which allow the possibility of dose titration should be given preference compared to SDSA.[20]

Favarel et al.,[21] in a study comparing CSA and SDSA use of 0.5% hyperbaric bupivacaine, showed that blood pressure lowered less in the CSA group compared to the SDSA group. The researchers found that the CSA group had less hemodynamic changes and that the slower start of segmental block and slow development of sympathetic block made adaptation easier.[21] De Andres et al.[22] used 0.5% isobaric bupivacaine in their comparison of CSA and SDSA and found hypotension due to the repeated dose in the CSA group did not need vasopressor drugs while the incidence of hypotension in the SDSA group was greater.

Klimscha et al.[18] compared 0.5% isobaric bupivacaine in CSA, SDSA and epidural anesthesia. Blood pressure in the CSA group did not reduce, in continuous epidural anesthesia there was a $15 \pm 3\%$ reduction and a $19 \pm 2\%$ decrease in the SDSA group. A comparison of SDSA with CSA by Reisli et al.[23] found a significant reduction in blood pressure in the SDSA group compared to the CSA group. Labaille et al.[24] used low dose 0.125% isobaric bupivacaine with CSA technique to provide effective anesthesia with minimal hemodynamic changes in older patients. Minville et al.[25] compared SDSA and CSA with low dose bupivacaine in planned hip operations in patients over 75 years. Occurrence of hypotension in the CSA group was 31% and 68% in the SDSA group; serious hypotension was 8% in the CSA group and 51% in the SDSA group. In the CSA group 4.5 ± 2 mg ephedrine was consumed, compared with 11 ± 2 mg in the SDSA group. They found the CSA group was hemodynamically more stable.

However Pitkanen et al.[26] compared CSA and SDSA techniques in planned hip and knee operations in 40 patients and found no significant difference in hemodynamic stability of the groups.

This study found both groups had lower blood pressure than the control values. In the CSA group 4% of patients developed hypotension compared to 12% in the SDSA group, subsequently the dose of ephedrine used was lower in the CSA group. The lower blood pressure in the SDSA group compared to the CSA group is similar to results from previous studies. Results from the use of levobupivacaine for CSA showed that it provides more hemodynamic stability than bupivacaine in CSA, in agreement with previously published research.

Patients under spinal anesthesia show a reduction in heart rate due to preganglion fiber blockage and a reduction in left atrium pressure.[8] Shenkman et al.[27] used low doses of local anesthetic with the CSA technique to provide good control of hemodynamics and this advantage over the SDSA technique made it suitable for use in older and more high risk patients. They found a maximum reduction in heart rate of 7.2% using 0.1% bupivacaine for CSA in ASA III–IV risk group patients. The researchers found that using CSA they could modify the sensory block level in a controlled fashion and reduce the risk of hemodynamic instability.[27] Favarel et al.[21] found no significant difference in heart rate using hyperbaric bupivacaine for CSA and SDSA. Similar research finding no significant difference in heart rate when using CSA compared to SDSA is available.[18,25,28] This study found no significant difference in heart rate between the CSA and SDSA groups at any time interval, similar to the literature.

Research evaluating CSA using levobupivacaine are limited. The only research in literature by Sell et al.[14] found the minimum effective dose of local anesthetic was 11.7 mg using levobupivacaine for CSA in hip replacement operations. Our study found an average dose of 8.7 mg levobupivacaine provided sufficient anesthesia. We are of the opinion that the difference may be due to demographics, position, intended block level and other such factors.

This study found the time to reach dermatome T10 sensory block level was significantly longer in the CSA group than the SDSA group. This is similar to times to reach sensory block levels that allow surgery in previous research.[21,22,29] While there was no significant difference in peak dermatome, the time for the CSA group to reach peak dermatome was significantly longer. This result conforms with previous studies.[18,28]

Comparing Bromage scale evaluations of motor block level the CSA group was significantly lower than the SDSA group. While motor block is a desirable characteristic in surgeries such as orthopedics, it delays neurologic evaluation postoperatively and obstructs mobilization. For this reason an early end to motor block is a desirable property. The lower degree of, and early end to, motor block in the CSA group could be seen as an advantage.

SDSA group patients required an average of 12.5 mg levobupivacaine compared to 8.7 mg for the CSA group. Though the CSA group used less local anesthetic, sufficient anesthetic level, similar to the SDSA group, was achieved.

No significant difference was found between the groups in terms of pain levels evaluated using VRS. While there was no difference in the two groups' use of morphine and number of time drugs were given by the PCA unit, there were significantly more requests from the PCA units by the CSA group 9, 18 and 24 h after the operation. We believe this may be due to greater complaints of back pain by the CSA

group compared to the SDSA group. It may also be due to the lower local anesthetic dose and lower nerve block level in the CSA group.

It is known that epidural and spinal anesthesia at different levels suppresses the neuroendocrine stress response better than general anesthetic. High level spinal block is necessary to suppress the andrenergic response.[30] Seitz et al.[31] found cortisol increased during surgery in lower extremity operations using general anesthetic, while the epidural anesthetic group had lower levels compared to values from before surgery. Pfug et al.[32] found higher levels of adrenalin postoperatively compared to control values. Low level spinal anesthesia prevents this increase, the high level spinal anesthetic group had values lower than the controls. While Moller et al.[33] found no difference in cortisol levels in the late postoperative period comparing spinal and general anesthesia, during surgery and in the early postoperative period cortisol levels were lower in the spinal anesthesia group. Comparing the postoperative plasma adrenalin and serum cortisol levels in both groups in this study, both groups had lower levels compared to control values. The SDSA group postoperative serum cortisol levels were significantly lower. The higher nerve block level in the SDSA group may be responsible for greater suppression of afferent neural impulses originating in the splanchnic sympathetic nerves.

In conclusion continuous spinal anesthesia using 0.25% concentration levobupivacaine to provide regional anesthesia for transurethral prostate resection operations in older patients can be used safely.

Conflict of interest

The authors declare no conflicts of interest.

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