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Comparison of haemodynamic parameters between the high and low spinal block in young healthy patients

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ABSTRACT

Background: For some surgical procedures a higher sensory block is needed. However, it is complicated by a higher incidence of hypotension, more bradycardia and nausea and a higher use of vasoactive drugs. In elderly and obstetric population complications have been attributed to the decrease in cardiac output and systemic vascular resistance, especially in a high block (above Th6). The aim of our study was to find the incidence of hypotension and bradycardia after a spinal anaesthesia in young, healthy patients. As young patients compensate more, we aimed to find the difference in haemodynamic variables between the group with a high and the group with a low spinal block and the underlying mechanisms of hypotension.

Methods: in a prospective, randomized study 44 ASA 1 patients scheduled for knee arthroscopy under spinal anaesthesia were randomly distributed to a high (group H) and a low (group L) spinal block group. In a group H patients were placed into horizontal, whereas in a group L in 15-degree anti-Trendelenburg position immediately after the spinal block. Haemodynamic parameters were measured continuously noninvasively from 10 min before to 25 min after the spinal block using the CNAPTM device with the LiDCORapid monitor.

Results: The differences in haemodynamic parameters between the groups were not statistically significant at all measured times despite a significant difference in the spinal block level (18.5 vs 13.3 dermatomes above S5, $p<0.001$) and a significant difference in haemodynamic variables inside each group compared to the baseline value. With cardiac index (CI) as a dependent variable, a significant correlation between CI and stroke volume index (SVI) was found ($\beta=0.849$, $p<0.001$) and also between CI and heart rate (HR) ($\beta=0.573$, $p<0.001$). In group H the incidence of hypotension was 35%, whereas in group L it was 10%. The same difference was seen in the use of phenylephrine between the groups, however the difference was not significant.

Conclusion: In our study it was found that in young, healthy patients there are no significant differences in haemodynamic parameters and in incidence of hypotension between a high and low spinal block. Young, healthy patients compensate a decrease in systemic vascular resistance caused by the spinal anaesthesia with a compensatory increase in CI resulting from an increase in SVI and HR. However, a trend towards less hypotension, less bradycardia and less frequent phenylephrine use in a low spinal block was noted.

Keywords: spinal anaesthesia, hyperbaric bupivacaine, haemodynamic parameters, cardiac output, hypotension

INTRODUCTION

Spinal anaesthesia is a safe and routinely used anaesthetic technique, however it is related to various haemodynamic changes in the patient, most commonly hypotension (1, 2). The incidence of hypotension with a higher spinal block (Th7 or higher) appears to be as high as 60% or even more in elderly and obstetric population (3-5). Hypotension may precede cardiac events (6) and increase 1-year postoperative mortality (7) therefore, many studies have focused on the prevention of hypotension due to spinal anaesthesia (8).

The underlying mechanism is the preganglionic sympathetic block and preserved or even increased parasympathetic nerve activity (9), leading to a decreased systemic vascular resistance (SVR) and venodilatation, which causes a peripheral venous pooling of blood. The consequence is a lower inflow of venous blood into the heart, a decrease in cardiac output (CO) and finally a decrease in arterial blood pressure (10, 11). Besides this, in higher spinal block the loss of sympathetically mediated cardiac stimulation decreases heart rate and stroke volume leading to further decreases in CO. Hypotension during a high spinal anaesthesia is thus a result of decreased CO and SVR (12). It has been shown that even if a decrease in CO was prevented (with application of colloids and/or phenylephrine), hypotension could not be prevented (13). This shows that CO is unable to compensate a simultaneous decrease in SVR and that the decrease in SVR could be the dominant mechanism for hypotension during a high spinal anaesthesia (14). On the other hand, there is considerably less hypotension in patients with a lower spinal block and the decreases in systolic arterial pressure (SAP) are modest (up to 20%). It is the consequence of the increase in sympathetic nervous system activity with a compensatory vasoconstriction in areas above

the spinal block (thorax, upper limbs) (15-17) and a partial increase in CO, caused by the increases in heart rate (HR) and stroke volume (SV) (18). Besides hypotension, the sympathetic block also causes bradycardia, nausea, vomiting, dysrhythmias and rarely cardiac arrest (1).

In previous studies it has been suggested that the incidence of hypotension depends on the level of spinal block and the age of the patient (1, 3, 4, 19). The correlation between hypotension and an intrathecal dose of local anaesthetics was found with low doses resulting in less hypotension, vasopressor requirement, and nausea, presumingly because of a lower cephalic spread of local anaesthetic and a lower reduction of systemic vascular resistance (20-22). Over 60 years ago, the difference in haemodynamic parameters between a high and low spinal anaesthesia was already noticed (the limit was Th4 dermatome), but no statistical analysis was performed (23). In a study by Asehnoune et al. (19), a significant difference in the change in CO was seen between two groups of patients with different sensory block levels: 6th and 8th thoracic vertebra. However, the study was performed on elderly and did not show a significant difference in the incidence of hypotension. Despite the above mentioned studies, the correlation between the spinal block level and the change in haemodynamic parameters has not been sufficiently investigated.

The majority of studies on haemodynamic changes in spinal anaesthesia were performed on elderly (above 60 years of age) and parturient, however their haemodynamic status may be influenced by other factors. Elderly patients have higher decreases in systemic vascular resistance during spinal anaesthesia compared to young patients (24, 25), some authors consider it as the main mechanism of hypotension in elderly (26), besides this, in the aged heart there is less of a compensatory increase in heart rate and contractility (decreased beta-adrenergic responsiveness), therefore a compensatory increase in cardiac output is smaller than in young adults or there is even a decrease in CO. On the other hand, the basal haemodynamic status of a healthy pregnant woman is characterized by a decrease in SVR, an increase in total blood volume and CO (27) and because of lower vascular tone, more blood volume is trapped in extremities (28). Besides this, pregnant women are more susceptible to the effects of the sympathetic block (29).

Another limitation of many published studies is that the primary outcome of many studies was the incidence of hypotension, which was recognized by an intermittent non-invasive measurement of arterial blood pressure without advanced haemodynamic monitoring (CO and SVR). In this way, many episodes of hypotension were missed (30).

Based on the above literature, we came to a conclusion that there is a lack of studies that would examine the haemodynamic changes during spinal anaesthesia in healthy, younger subjects, which could provide the data for a better insight into the mechanisms of hypotension and would support the efforts to prevent it.

This is the first study in young healthy non-obstetric patients that compares a high to low spinal block with the same dose of hyperbaric local anaesthetic using the continuous non-invasive recording of haemodynamic parameters. We hypothesized that different levels of the spinal block would result in significant differences in haemodynamic variables.

MATERIALS AND METHODS

In our prospective, randomized, single-blinded study 44 American Society of Anaesthesiologists (ASA) 1, patients aged between 18 and 40 years were included. Patients receiving spinal anaesthesia for knee arthroscopy between January 2014 and October 2015 were included in this study. The exclusion criteria included: chronic diseases (including peripheral arterial disease (PAD), Raynaud's syndrome and vascular surgery of the upper extremities; disorders of heart rhythm), drugs that could influence the patient's haemodynamic status, contraindications to spinal anaesthesia, patient's refusal to participate in the study, a history of allergy to local anaesthetic and a conversion to general anaesthesia.

All patients were informed about the study and gave a written consent. Premedication was performed with 7.5mg of oral midazolam and patients were allowed to drink clear liquids up to 2 h before surgery. On arrival to the operating theatre, an 18-gauge intravenous cannula was inserted in a peripheral vein on the arm, not used for measurements. Standard monitoring (pulse oximetry, ECG, oscillometric upper-arm non-invasive blood pressure) was applied and connected with a Dräger Infinity Delta monitor (Drägerwerk AG & Co. KGaA, Lübeck, Germany). According to the risk/benefit ratio, the method of haemodynamic monitoring for a healthy patient population should be non-invasive (31) and according to availability at our institution the LiDCORapid monitor with CNAP was used. Therefore, the LiDCORapid v2 (LiDCO Ltd., Cambridge, United Kingdom) with CNAPTM monitoring system (CNSystems Medizintechnik AG, Graz, Austria) was applied on an index and middle finger on an arm without an intravenous cannula. The CNAPTM device develops an arterial waveform noninvasively by applying exterior pressure to the finger vessel wall keeping the blood volume of the finger arteries constant. The pressure in the cuff, which is needed to keep the volume constant, corresponds to arterial pressure. It is calibrated intermittently with a NIBP cuff.

The baseline measurements of haemodynamic parameters were performed after 10 minutes of lying in a supine position (systolic arterial pressure – SAP, mean arterial pressure – MAP, cardiac index - CI, systemic vascular resistance index - SVRI, stroke volume index – SVI and pulse pressure - PP). SVRI was calculated by the formula: SVRI = 80 x (MAP – RAP) / CI (by LiDCORapid), where RAP is the right atrial pressure. A RAP value was arbitrarily set to 7 mm Hg; namely, with non-invasive methods it was not possible to measure its real value.

After the measurement, a spinal anaesthesia was performed in a sitting position at the L2-L3 or L3-4 interspace using a 26G atraumatic spinal needle with introducer (Atraucan, B. Braun Medical, Melsungen, Germany). In each patient 12,5 mg of hyperbaric bupivacaine 0.5% (Marcaine Spinal Heavy; Astra Zeneca, Lund, Sweden) was injected intrathecally over 30s and the patient was immediately placed in a supine position.

After anaesthetic administration, the patients were randomized into 2 groups: group H (high spinal block) and group L (low spinal block) by the method of sealed envelopes (each envelope contained a number, generated by a computer and a paper saying "high" or "low block"). All spinal blocks were performed by the same experienced anaesthesiologist. In group H, the patient was put in a supine position with the operating table in horizontal position after the induction of subarachnoid block, whereas in group L the table was

tilted approximately 15 degrees in anti-Trendelenburg position for 10 minutes and then into horizontal supine position. The upper sensory level of spinal block was evaluated for 10 min in 2-minute intervals and in 5-minute intervals for another 20 min until there was no change in 3 consecutive readings. It was measured as a loss of cold sensation (using a sponge immersed in ice-cold alcohol). The haemodynamic variables were measured constantly with a recalibration each 5 min. A finger-cuff was switched from the index to middle finger and the opposite way each 20 min, as instructed by the CNAP company. An arm with the CNAP device was wrapped in warm swabs to prevent vasoconstriction because of low operating theatre temperatures and instructions were given to patients to keep the arm still. Time measurement started with the withdrawal of the spinal needle.

Before the induction of spinal anaesthesia all patients received 2g of cefazolin in 100ml of saline over 15 min, after which an infusion of lactated Ringer's solution (5mL/kg/h) was started.

Hypotension was defined as SAP less than 80% of baseline – the value accepted by most investigators (32-34). In case of hypotension, a bolus of 100 mcg of intravenous phenylephrine was given as a rescue medication with no additional fluid. If there was concomitant bradycardia (heart rate < 50 beats/min), a bolus of 0.5 mg atropine was given. The anaesthesiologist performing the block and measuring the sensory block level was blinded for the haemodynamic measurements. The monitoring of the patient as well as fluid and drug requirements were managed by another anaesthesiologist, blinded for the spinal block level.

The primary objective of our study was to determine the difference in CI values and in the incidence of hypotension between the patients with a high and the patients with a low spinal block. The decision to use the CI as the primary variable was based on the literature showing that inadequate CO results in reduced organ perfusion and an impaired microcirculation (35). The secondary outcome was to observe the incidence of complications (nausea).

STATISTICAL ANALYSIS

The haemodynamic measurements were stored in the LiDCORapid monitor and downloaded as .csv files for each patient. The beat-to-beat data set was transformed into average values every 30 s. The data for the first 3 minutes after the spinal block were inconsistent because of a change in the patient's position from sitting to a supine, therefore those data were omitted.

For the purpose of statistical analyses, dermatome levels were scored in sequence, starting at the 5th sacral segment (S5) with number 1.

SPSS statistical program v.17.0 was used for the analysis of all data. The data were expressed as means, 95% confidence intervals for means or as a number of patients and percentage.

For a normal distribution of the data, Kolmogorov-Smirnov test was used. The Paired Sample T-test was used to detect haemodynamic parameters' changes compared to the baseline values of the parameters, Independent Sample T-test to test the difference between the study groups and Multiple linear regression analysis to assess the relationship between the patient characteristics and baseline parameters with a change in CI, SAP, MAP, SVRI and HR. Chi-square test was used to compare the proportions of hypotension, nausea and the need for vasoactive drugs between the two groups. $P < 0.05$ was considered as statistically significant.

According to preliminary data and the data from the literature (19), a sample size of 20 patients per group was determined as sufficient to detect a 25% difference in cardiac index between high and low spinal anaesthesia group (SD 0,9 L/min/m2) with a power of 80% and the probability level of 0.05. To allow for a possible dropout rate of 10%, we needed 44 patients in this study.

The study was approved by Slovenian Medical Ethics Committee (Ref.: 175/02/10).

RESULTS

Forty-four patients referred to knee arthroscopy were randomly distributed in 2 groups receiving high or low spinal anaesthesia. One patient showed excessive movement of the fingers due to anxiety, whereas 3 additional patients were excluded from data analyses because of problems with haemodynamic monitor calibrations. Therefore, 40 patients were included in the analysis with 20 in each study group.

The variables in the majority of observed events and repeated measurements were distributed normally, the assumption that the data were distributed normally was confirmed (Table 1).

Both groups had comparable demographic data (age, BMI, gender and height) and the baseline values of haemodynamic parameters (CI, SAP, MAP, SVRI, PP and HR) prior to spinal anaesthesia (Table 2).

The level of sensory block was significantly higher in group H compared to group L (18.5 (95%CI 17.9-19.1) vs 13.3 (95%CI 12.7-13.9) dermatomes above S5, $p<0.001$) or converted into spinal segments 10th vs. 5th thoracic vertebral segment. The average time to reach the maximal level of sensory block was significantly longer in group H than in group L (12.8 (95%CI 11.4-14.2) vs. 10.9 (95%CI 10.2-11.6) min, $p=0.026$).

The primary outcome in our study was the change in CI values after different levels of spinal anaesthesia. In group H the values of CI were significantly higher at all measurement periods (5, 10, 15, 20 and 25 min) after the spinal block compared to the baseline value (Table 3, Figure 1). To contrast, a significant increase in CI was seen only 5 minutes after the spinal block in group L with respect to the baseline value, whereas at 10, 15, 20 and 25 minutes after the block the increase in CI compared to baseline was not significant. At all times the values of CI were above baseline in both groups. No significant difference in CI was found between the groups at any time ($p=0.946$) (Table 3).

A significant decrease in a SAP was seen at all times after the spinal block in group H compared to the baseline value, whereas in group L the decrease was significant at 10 min or later after the spinal block (Table 3, Figure 2). Comparing both groups of patients, no significant difference in SAP change with respect to the baseline values was found between the groups at any time ($p=0.289$). Concomitantly, a significant decrease in MAP and SVRI values with respect to baseline was seen in both groups at all measurements. As for SVI, there was a significant increase in SVI values at 15 minutes or later after the block in group H and at all measured times in group L. In no patient a MAP value < 60mmHg was recorded. Heart rate values were significantly increased compared to baseline only 5 minutes after the block in group H, later the difference was not significant. In group L a significant decrease in HR was seen at 15 minutes or later after the block. Comparing both studied groups, no significant difference was found in any of the meas-

ured haemodynamic parameters between the groups at any time.
With independent variables (SVRI, SVI, PP, HR) we were able to explain 98.7% of CI as a dependent variable (R2=0.987, R=0.993, p<0.001). A significant correlation between CI and SVI was found (β=0.849, p<0.001) (Figure 3) and also between CI and HR (β=0.573, p<0.001) (Table 4). With other haemodynamic parameters no significant correlation was found, also no correlation was found with the level of sensory block (R2=0.006, R=0.077, p=0.622). With SAP as a dependent variable, a significant correlation was only found between SAP and pulse pressure (R2=0.681, R=0.825, p=0.004, B=0.686, β=0.738, p<0.001), with MAP there was no correlation. Also, no significant correlation between the decrease in SAP and the level of sensory block was found (R2=0.001, R=0.032, p=0.845).

The overall incidence of hypotension in our study was 22,5% (9/40 patients), with 35% (7/20) in group H and 10% (2/20) in group L, however the difference between the groups was not significant (p=0.064). All patients with hypotension received 1 bolus of 100 mcg of phenylephrine, resulting in 7 doses of phenylephrine in group H and 2 in group L, again the difference between the groups was not significant (p=0.064). A significant correlation between the phenylephrine consumption and sensory block level was found (Pearson correlation coefficient (ρ) = 0.367, p=0.020). There was a trend of higher incidence of nausea in group H, however the difference was not significant (Table 5). No patient vomited during the study.

DISCUSSION

In this prospective randomized study, we found no significant difference in haemodynamic parameters between high and low spinal anaesthesia in young, healthy subjects, with which our hypothesis was disproved. However, there was a trend of advanced haemodynamic instability in patients with a high spinal block. Also, the differences in the incidence of hypotension were not statistically significant between the groups of patients.
To our knowledge, this is the first study that studied the influence of spinal anaesthesia level on haemodynamic variables in healthy, young, non-pregnant participants using non-invasive, continuous measurement method. Both study groups were similar in terms of age, gender, height, BMI, time to maximal sensory level of spinal block and baseline values of haemodynamic parameters.
The level of sensory block was significantly higher in group H compared to group L, which was accomplished with the use of the same dose of hyperbaric bupivacaine (12,5mg) in both groups. The difference in the level of sensory block was achieved by the tilt of the operating table with a slight anti-Trendelenburg position in group L. It was shown before that with the positioning of the patient, different levels of sensory block could be achieved (36-38). We decided for the dose of hyperbaric bupivacaine that is high enough to produce high spinal block (12,5mg), even in young patients. Namely, in young patients, the sensory block level after subarachnoid injection of hyperbaric local anaesthetic solution is usually 3-4 spinal segments lower than in elderly (19, 39, 40). Hyperbaric bupivacaine was chosen as it is easier o get the reliable spinal block level (41). In our patients (in group H) a higher spinal block was applied as would be required by the surgical procedure, however it was performed on ASA 1 population with a normal compensatory reserve, patients who could well tolerate haemodynamic shifts caused by high spinal anaesthesia.
In most studies, different levels of spinal block were achieved through different dosages of local anaesthetic (19-22, 42, 43) and/or different baricity of local anaesthetics (44). The conclusion of majority of studies was that with a lower dose of the local anaesthetic patients were more haemodynamically stable and that it was most probably the consequence of a different level of sympathetic block (45, 46). The drawback of lowering the doses (<5mg) was the increasing incidence of spinal block failures with pain, slower onset and shorter duration of the block and also the increasing rate of conversions into general anaesthesia (42, 44, 47, 48). In contrast to the above mentioned studies, Langesaeter et al. (20) showed that there was a difference in the incidence of hypotension with the same sensory block level, but a different local anaesthetic dosage. According to the above described findings, the focus of our study was the level of spinal block as the underlying factor for the difference in haemodynamic parameters during a spinal anaesthesia excluding different doses and/or baricities of local anaesthetic.
A mean time to maximum level of sensory block was 12.8 minutes for group H and 10.9 minutes for group L. The timings are comparable to previous studies with a mean time of 15 minutes and a range 11-20 minutes (49, 50).
The primary outcome of our study was the difference in CI value change between the group of patients with a high and the group with a low spinal block. CI is a primary determinant of global oxygen transport from the heart to the body (51), therefore it was chosen as a primary outcome. In group H a significant increase in CI was found at all times. In group L there was a significant increase in CI values only 5 minutes after the block. Because of a lower block of sympathetic nerves in group L less compensatory increase in CI was necessary leading to insignificantly higher values of CI (above baseline) in this group 10 minutes or more after spinal anaesthesia. CI values in all patients were above baseline at any time after the spinal block. Also, in the study by Dyer et al. (18), it was shown that there is an increase in CI during a spinal anaesthesia, which could be caused by the increases in HR and SV. These findings were confirmed by our study, where a significant correlation between an increase in CI and an increase in SV and a correlation between an increase in the CI values and an increase in HR was found. The most probable reason for a CI increase is compensatory response to a significant decrease in a SVRI value (at the same time SVI increased significantly), but it could also be attributed to the change of the patient's position from sitting to supine. What is more, the haemodynamic curves showed the most prominent decrease in SVRI with a concomitant increase in CI in the first 5 minutes after the spinal block in group H and group L, with a peak effect after approximately 4 minutes. Similar findings were published by Langesaeter et al. (20), who found maximal change in cardiac output and systemic vascular resistance 3 minutes after the spinal block, however, in their study a lower dose of isobaric bupivacaine was used.
When we compared the increase in CI values between group H and group L, no significant difference was noted at all measured times. Most probably the lack of significance between the groups was the consequence of strong compensatory mechanisms (vasoconstriction) in the regions above the block and an increase in SVI and HR, which is more prominent in

young patients. Compensatory vasoconstriction was probably more prominent in group H, however, we did not measure the sympathetic activity (e.g. by heart rate variability) to prove the theory (17). Another possible factor could be the insufficient difference in spinal block level to show the difference in haemodynamic parameters in young, healthy patients, also, the block was not high enough to prevent a compensatory vasoconstriction in the non-blocked areas. Besides this, all episodes of hypotension were promptly treated, preventing significant changes from happening. Our findings are in contrast to Asehnoune, who found significant difference in changes of CO values between the group of patients with the spinal block up to Th6 and the group up to Th8. However, their study was performed on elderly and also ASA 2 patients. It has been shown before that elderly patients have larger decreases in systemic vascular resistance during spinal anaesthesia compared to young patients (24, 25) and a decreased beta-adrenergic responsiveness.

Systolic arterial pressure and MAP decreased significantly after the spinal anaesthesia in both treatment groups, only in group L the decrease in SAP was not significant 5 minutes after the spinal block. However, the difference between the groups in the change of SAP and MAP values was not significant at any time. No episode of MAP below 60mmHg was recorded. These results show that despite the significant increase in CI, the decrease in SVRI could not be compensated for and the consequent drop in SAP and MAP could not be prevented, except in group L 5 minutes after the spinal block. The decrease in SAP>20% (hypotension) was found in 22.4% patients, higher in group H (35%) compared to group L (10%), however, the difference was not statistically significant. In each subject with hypotension there was only 1 episode of hypotension, responsive to vasoactive drugs. The overall incidence of hypotension was low, which could be attributed to a relatively low block and compensatory mechanisms in young subjects. In a recent study Lawicka et al. (52) showed that in patients aged around 40-years of age ASA status 1 and 2, the incidence of hypotension with the spinal block around 6th thoracic segment was 39%. The incidence of hypotension was similar to our group H in which spinal block level was around Th4, although a much lower dose of hyperbaric bupivacaine was used in our study. It suggests that hypotension could depend on spinal anaesthesia level, despite different doses of local anaesthetic. Carpenter et al. (1) defined the spinal block above the level of 5th thoracic vertebra as the risk factor for hypotension in non-obstetric population. The studies on obstetric population showed an incidence of hypotension as high as 81% (53-56), which was the consequence of a high spinal block (above Th6 or even Th4) and higher susceptibility of pregnant women to the effects of sympathetic block (29).

The incidence of bradycardia in our study was 7.5% with bradycardia only in group H. The incidence was lower than in the study by Lesser et al. (57), because in our study there was no bradycardia in group L. If we took into account only group H, the incidence was 15%, which was higher than published before. This was most probably the consequence of a higher spinal block, the average patients' age below 37 years, ASA1 and elective surgery, risk factors acknowledged also by other authors (1, 57). The initial increase in HR 5 minutes after the block was most probably a compensatory response to a decrease in SVRI and it was probably also the consequence of a diminished parasympathetic activity to the heart (9, 18). Cook et al. (9) showed an initial increase in HR of 6-8% after the spinal block, which was higher than in our study (5%). In group L, a significant decrease in HR occurred after 15 min, which matched the time to the maximal spinal block and was the consequence of a sympathetic block.

All patients in our study received only a maintenance infusion of crystalloids to avoid the influence of fluids on haemodynamic parameters and to decrease the probability of urine retention. Despite this, the incidence of hypotension was low and it was treated with phenylephrine. The decision for the phenylephrine was based on the mechanism of hypotension (the decrease in SVR) and the safety and efficacy of the drug (58). With the use of phenylephrine boluses, it was easier to keep the values of haemodynamic parameters closer to baseline values (59), as it had a faster onset and could be more accurately titrated than other vasoactive drugs (60).

Besides hypotension, other common side-effects related to hypotension were nausea, vomiting, and dizziness with incidences of around 25% (61). In our study, the incidence of nausea in group H was 25%, whereas in group L it was 5%, the difference between the groups was not significant.

Haemodynamic parameters in our study were measured using CNAPTM (continuous non-invasive arterial pressure) in combination with a LiDCO Rapid monitor. It was shown before that cardiac output and stroke volume were more valuable for detecting haemodynamic changes than conventional non-invasive monitoring (NIBP) (62). The CNAPTM device has been used as arterial pressure monitoring in patients with a spinal anaesthesia before (63) and it has detected more hypotensive episodes after a spinal anaesthesia than intermittent blood pressure devices (NIBP). Besides, a rigorous anaesthesia clinical trial showed real time estimates of arterial pressure by CNAP were comparable with an invasive arterial pressure (64), a gold standard of invasive measurements. In spontaneous breathing, low-risk patients invasive monitoring using arterial line would not be ethically justified (65). According to our experience, a CNAP device has failures in recordings and needs recalibration more often than the 20-min intervals, advised by the manufacturer. We also followed the advice from the company to synchronize a NIBP cuff of the main patient monitor with the CNAP device. The PulseCO algorithm that was used in analysis of arterial pressure curve by LiDCORapid monitor, has been validated and used in healthy, pregnant patients receiving spinal anaesthesia (66, 67). The absolute value of CI measured with this method has been controversial, however its value for monitoring the trends in CI values has been validated and accepted, also in spinal anaesthesia (30, 63, 68). We were aware of the limitations of the method used in the assessment of absolute values of CI; also in SVRI calculations the mean atrial pressure was not measured but arbitrarily set to 7 mmHg.

The strengths of our study: after a rigorous literature review, it appears that this is the first prospective randomized study on spinal anaesthesia in young, healthy patients with two different levels of spinal block. The study will certainly add to knowledge and will form the basis for future research in risk factors for hypotension during spinal anaesthesia and its prevention.

Our study had several limitations. The method used to measure haemodynamic parameters (CNAP) was susceptible to patient movement and low operating theatre

air temperature. Besides this, the patient position was changed from sitting to supine after spinal anaesthesia influencing haemodynamic measurements in the first 5 minutes. Additionally, patients in group L were tilted anti-Trendelenburg position for the first 10 minutes probably causing more prominent compensatory vasoconstriction in the areas above the spinal block. The study involved a relatively small number of patients (it was powered to the difference in CI and not the other variables), which may impact the generalizability of the results. Also, it was only single blinded, as the researcher could not be blinded to block level, which adds to selection bias.

CONCLUSIONS

In young, healthy patients no significant difference was found in haemodynamic parameters between a group with a high and a group with a low level of sensory block using the same dose of hyperbaric bupivacaine. However, a trend towards less hypotension, less bradycardia and less frequent phenylephrine use in low spinal block was seen. This study proves that the main mechanism of hypotension in spinal anaesthesia is the decrease in systemic vascular resistance, however, young, healthy patients compensate much higher levels of spinal anaesthesia than other population. A possible strategy for reducing spinal anaesthesia induced hypotension and other haemodynamic deterioration according to our study still remains to minimize the peak block level to as low as possible for the planned procedure, which can be achieved only by adjusting the patient position. However, determining the most appropriate preventive measure and finding the risk factors for hypotension in young, healthy patients remains to be further studied.

CONFLICT-OF-INTEREST STATEMENT

All physicians involved in this study were staff members of the Department of Anaesthesiology and Intensive Care, University Medical Centre Ljubljana, Slovenia. Monitoring, equipment, and medication used during the study were those routinely used for anaesthesia in our hospital. CNAPTM system was a part of equipment at our clinical department. There are no conflicts of interest by all authors.

Table 1. The Kolmogorov-Smirnov and Shapiro-Wilk test of a normality of the distribution of the data in patients with high (group H) and patients with low (group L) sensory block.

		Kolmogorov-Smirnov			**Shapiro-Wilk**		
	Group	Statistic	df	Sig.	Statistic	df	Sig.
CI beginning	L	,108	20	,200*	,977	20	,886
	H	,135	20	,200*	,982	20	,956
CI after 5 min	L	,154	20	,200*	,943	20	,269
	H	,175	20	,110	,866	20	,010
CI after 10 min	L	,107	20	,200*	,979	20	,925
	H	,172	20	,124	,958	20	,508
CI after 15 min	L	,183	20	,079	,956	20	,473
	H	,117	20	,200*	,977	20	,894
CI after 20 min	L	,129	20	,200*	,975	20	,851
	H	,108	20	,200*	,963	20	,614
CI after 25 min	L	,158	20	,200*	,967	20	,690
	H	,147	20	,200*	,947	20	,320
SAP beginning	L	,143	20	,200*	,950	20	,367
	H	,099	20	,200*	,980	20	,935
SAP after 5 min	L	,151	20	,200*	,960	20	,545
	H	,122	20	,200*	,960	20	,553
SAP after 10 min	L	,088	20	,200*	,985	20	,983
	H	,182	20	,082	,912	20	,071
SAP after 15 min	L	,163	20	,173	,948	20	,336
	H	,100	20	,200*	,989	20	,996
SAP after 20 min	L	,090	20	,200*	,978	20	,903
	H	,108	20	,200*	,951	20	,390

SAP after 25 min	L	,150	20	,200*	,952	20	,395
	H	,124	20	,200*	,978	20	,899
MAP after 5 min	L	,159	20	,200*	,923	20	,115
	H	,162	20	,179	,958	20	,505
MAP after 10 min	L	,094	20	,200*	,983	20	,970
	H	,183	20	,078	,906	20	,053
MAP after 15 min	L	,118	20	,200*	,964	20	,629
	H	,140	20	,200*	,966	20	,677
MAP after 20 min	L	,124	20	,200*	,968	20	,715
	H	,249	20	,002	,904	20	,049
MAP after 25 min	L	,161	20	,189	,950	20	,362
	H	,179	20	,094	,937	20	,210
SVRI beginning	L	,224	20	,010	,834	20	,003
	H	,143	20	,200*	,927	20	,132
SVRI after 5 min	L	,173	20	,117	,956	20	,474
	H	,179	20	,092	,878	20	,016
SVRI after 10 min	L	,129	20	,200*	,928	20	,141
	H	,238	20	,004	,892	20	,030
SVRI after 15 min	L	,175	20	,112	,865	20	,010
	H	,198	20	,038	,841	20	,004
SVRI after 20 min	L	,245	20	,003	,810	20	,001
	H	,161	20	,184	,829	20	,002
SVRI after 25 min	L	,208	20	,023	,829	20	,002
	H	,163	20	,171	,853	20	,006
SVI beginning	L	,192	20	,051	,899	20	,039
	H	,139	20	,200*	,914	20	,075
SVI after 5 min	L	,213	20	,018	,830	20	,003
	H	,082	20	,200*	,979	20	,914
SVI after 10 min	L	,149	20	,200*	,886	20	,023
	H	,167	20	,146	,939	20	,229
SVI after 15 min	L	,143	20	,200*	,915	20	,080
	H	,089	20	,200*	,965	20	,639
SVI after 20 min	L	,161	20	,189	,939	20	,225
	H	,120	20	,200*	,955	20	,442
SVI after 25 min	L	,152	20	,200*	,930	20	,153
	H	,152	20	,200*	,924	20	,118
PP beginning	L	,159	20	,200	,907	20	,055
	H	,176	20	,106	,904	20	,049
PP after 5 min	L	,131	20	,200*	,970	20	,758
	H	,111	20	,200*	,972	20	,800
PP after 10 min	L	,114	20	,200*	,956	20	,465
	H	,170	20	,131	,913	20	,072
PP after 15 min	L	,188	20	,061	,923	20	,113
	H	,121	20	,200*	,960	20	,548
PP after 20 min	L	,118	20	,200*	,943	20	,278
	H	,119	20	,200*	,968	20	,721

PP after 25 min	L	,126	20	,200*	,943	20	,277
	H	,161	20	,188	,939	20	,231
HR beginning	L	,099	20	,200*	,972	20	,800
	H	,140	20	,200*	,916	20	,083
HR after 5 min	L	,108	20	,200*	,953	20	,410
	H	,100	20	,200*	,966	20	,678
HR after 10 min	L	,164	20	,164	,945	20	,295
	H	,100	20	,200*	,978	20	,901
HR after 15 min	L	,102	20	,200*	,981	20	,946
	H	,148	20	,200*	,925	20	,123
HR after 20 min	L	,127	20	,200*	,935	20	,195
	H	,100	20	,200*	,984	20	,975
HR after 25 min	L	,172	20	,124	,932	20	,168
	H	,099	20	,200*	,972	20	,804

CI = Cardiac index, SAP = systolic arterial pressure, MAP = mean arterial pressure, SVRI = systemic vascular resistance index, SVI = stroke volume index, PP = pulse pressure, HR = heart rate

Table 2. The presentation of demographic, general data and baseline values of haemodynamic parameters in patients with high (group H) and patients with low (group L) sensory block. Data are presented as means (95% confidence interval for means) or a number of patients (%).

	Group H	**Group L**	**p-value**
Age (years)	31.8 (28.7-34.9)	34.3 (31.3-37.3)	0.271
BMI (kg/m2)	26.4 (25.5-27.3)	25.0 (23.7-26.3)	0.078
Sex (M/F)	13/7 (65%/35%)	11/9 (55%/45%)	0.374
Body height (cm)	175.6 (171.9-179.3)	173.1 (169.8-176.4)	0.340
No. of blocked dermatomes (sensory block) above S5	18.5 (17.9-19.1)	13.3 (12.7-13.9)	<0.001
Time to peak sensory block (min)	12.8 (11.4-14.2)	10.9 (10.2-11.6)	0.026
CI (L/min/m2)	3.14 (2.82-3.46)	3.27 (2.88-3.66)	0.603
SAP (mmHg)	131.4 (126.9-135.9)	131.8 (127.3-136.3)	0.891
MAP (mmHg)	96.2 (92.2-100.2)	98.8 (94.9-102.7)	0.364
SVRI (dyne*s/cm5*m2)	2457.2 (2164.5-2749.9)	2449.6 (2079.7-2819.5)	0.975
SVI (mL/m2/beat)	45.1 (40.9-49.3)	46.0 (41.2-50.8)	0.772
PP (mmHg)	53.5 (49.5-57.5)	53.8 (49.5-58.1)	0.920
HR (beat/min)	70.2 (65.6-74.8)	71.5 (66.6-76.4)	0.707

BMI = body mass index, CI = Cardiac index, SAP = systolic arterial pressure, MAP = mean arterial pressure, SVRI = systemic vascular resistance index, SVI = stroke volume index, PP = pulse pressure, HR = heart rate

Table 3. Haemodynamic parameters' values at Baseline, 5, 10, 15, 20, and 25 minutes after the spinal anaesthesia in patients with a high (group H) and patients with a low (group L) sensory block. The data are presented as means (95% confidence interval for means).

	Baseline	**5 min after the block**	**10 min after the block**	**15 min after the block**	**20 min after the block**	**25 min after the block**
CI (L/min/m2)						
Group H	3.14 (2.82-3.46)	3.40 (2.98-3.82)*	3.49 (3.05-3.93)*	3.58 (3.18-3.98) †	3.59 (3.13-4.05) †	3.60 (3.13-4.07)*
% change		8.5 (0.4-16.6)	11.0 (4.0-18.0)*	13.9 (8.3-19.5) †	13.6 (5.9-21.3)*	14.3 (5.6-23.0)*
Group L	3.27 (2.88-3.66)	3.61 (3.26-3.96)*	3.42 (3.05-3.79)	3.44 (3.09-3.79)	3.46 (3.10-3.82)	3.49 (3.12-3.86)
% change		13.7 (4.6-22.8)*	6.3 (-0.6-13.2)	7.6 (-1.5-16.7)	8.0 (-1.8-17.8)	9.4 (-1.9-20.7)

SAP (mmHg)						
Group H	131.4 (126.9-135.9)	126.2 (120.0-132.4)*	122.9 (116.7-129.1)*	121.1 (117.2-125.0)†	121.6 (116.9-126.3)†	121.6 (116.8-126.4)†
% change		-3.9 (-7.4- -0.4)*	-6.3 (-10.3- -2.3*	-7.6 (-10.2 - -5.0)*	-7.3 (-10.1- -4.5)*	-7.3 (-10.5- -4.1)*
Group L	131.8 (127.3-136.3)	131.6 (126.7-136.5)	126.7 (121.6-131.8)*	126.8 (121.8-131.8)*	123.4 (118.7-128.1)†	124.0 (119.3-128.7)*
% change		-0.0±6.7	3.8 (1.1-6.5)*	-3.7 (-6.6 - -0.8)*	-6.2 (-9.0- - 3.4)*	-5.7 (-8.8- -2.6)*
MAP (mmHg)						
Group H	96.2 (92.2-100.2)	87.7 (83.5-91.9)*	85.2 (80.7-89.7) †	84.4 (80.3-88.5) †	82.9 (78.8-87.0) †	83.7 (79.6-87.8) †
% change		-8.4 (-12.9- -3.9)*	-11.0 (-16.0- -6.0)*	-11.9 (-16.1- -7.7)*	-13.6 (-17.7- -9.5)*	-12.7 (-16.6- -8.8)*
Group L	98.8 (94.9-102.7)	92.4 (87.8-97.0) †	88.8 (84.2-93.4) †	88.8 (83.7-93.9) †	86.6 (81.7-91.5) †	86.2 (81.2-91.2) †
% change		-6.4 (-9.7- -3.1)*	-10.2 (-13.1- -7.3)*	-10.1 (-14.2- -6.0)*	-12.4 (-16.2- -8.6)*	-12.7 (-16.6- -8.8)*
SVRI (dyne*s/cm5*m2)						
Group H	2457.2 (2164.5-2750.0)	2091.8 (1802.4-2381.2) †	2048.6 (1750.6-2346.6) †	2043.8 (1738.4-2349.2) †	2016.6 (1676.9-2356.3) †	2004.7 (1667.8-2341.6) †
% change		-14.4 (-20.8- -8.0)†	-17.0 (-22.3- -11.7)†	-17.0 (-22.5- -11.5)†	-18.7 (-25.0- -12.4)†	-19.3 (-25.6- -13.0)†
Group L	2449.6 (2079.7-2819.5)	2016.8 (1767.7-2265.9)*	2143.2 (1820.3-2466.1)*	2124.6 (1778.7-2470.5)*	2045.7 (1688.6-2402.8)*	2044.8 (1674.7-2414.9)*
% change		-15.3 (-22.5- -8.1)*	-11.5 (-18.3- -4.7)*	-12.1 (-19.6- -4.6)*	-15.5 (-23.1- -7.9) †	-15.7 (-24.0- -7.4) †
SVI (mL/m2/beat)						
Group H	45.1 (40.9-49.3)	46.2 (41.3-51.1)	46.4 (41.0-51.8)	50.3 (44.6-56.0)*	52.5 (45.7-59.3)*	53.8 (46.7-60.9)*
% change		3.8 (-5.0-12.6)	2.8 (-4.5-10.1)	11.6 (4.1-19.1)*	16.5 (6.0-27.0)*	19.4 (8.0-30.8)*
Group L	46.0 (41.2-50.8)	51.0 (45.6-56.4)*	49.3 (43.2-55.4)*	51.5 (44.9-58.1)*	53.2 (46.6-59.8) †	54.2 (47.2-61.2) †
% change		12.3 (4.0-20.6)*	7.1 (0.6-13.6)*	12.0 (3.7-20.3)*	15.8 (6.9-24.7)*	17.8 (7.9-22.7)*
PP (mmHg)						
Group H	53.5 (49.5-57.5)	54.3 (49.0-59.6)	52.0 (46.3-57.7)	52.3 (47.4-57.2)	54.5 (49.5-59.5)	54.3 (49.2-59.4)
Group L	53.8 (49.5-58.1)	60.8 (56.7-64.9) †	57.2 (52.3-62.1)	57.3 (52.7-61.9)	56.5 (51.2-61.8)	57.8 (52.7-62.9)
HR (beat/min)						
Group H	70.2 (65.6-74.8)	73.9 (68.5-79.3)*	74.2 (69.4-79.0)	70.1 (65.8-74.4)	67.5 (63.5-71.5)	66.7 (62.8-70.6)
Group L	71.5 (66.6-76.4)	72.0 (67.6-76.4)	70.3 (65.9-74.7)	67.4 (63.1-71.7)*	65.4 (61.4-69.4) †	65.8 (61.1-70.5)*

CI = Cardiac index, SAP = systolic arterial pressure, MAP = mean arterial pressure, SVRI = systemic vascular resistance index, SVI = stroke volume index, PP = pulse pressure, HR = heart rate

* $p < 0.05$ with respect to baseline

† $p < 0.001$ with respect to baseline

Table 4. Regression analysis with cardiac index (CI) as dependent variable and other haemodynamic parameters as independent variables.

	B	Beta	t-value	p-value
constant	-3,130		-7,949	0,000
SVRI	0,000	0,022	0,498	0,622
SVI	0,067	0,849	21,232	0,000
PP	0,003	0,035	1,530	0,135
HR	0,043	0,573	18,911	0,000

CI = Cardiac index, SVRI = systemic vascular resistance index, SVI = stroke volume index, PP = pulse pressure, HR = heart rate

Table 5. The frequency distribution of hypotension, bradycardia, atropine and ephedrine consumption in patients with a high (group H) and patients with a low (group L) sensory block. The data are presented as number of patients (%).

	Group H (n=20)	Group L (n=20)	p-value
Hypotension	7 (35%)	2 (10%)	0.064
Bradycardia	3	0	0.115
Phenylephrine requirement	7 (35%)	2 (10%)	0.064
Atropine requirement	3	0	0.115
Nausea	5 (25%)	1 (5%)	0.091

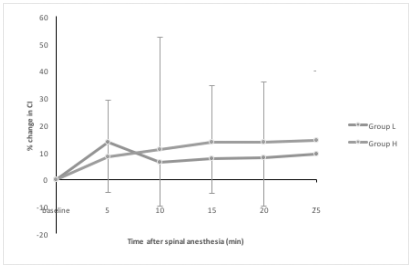

Figure 1: Time course of percentage of change in cardiac index (CI) with respect to baseline in patients with a high (group H) and patients with a low (group L) sensory block.

CI = cardiac index
*p < 0.05 with respect to baseline
†p < 0.001 with respect to baseline

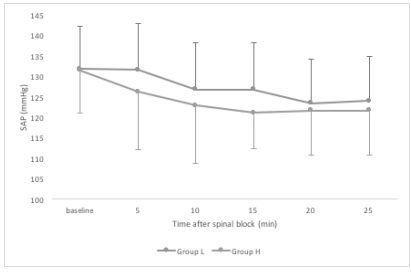

Figure 2: Time course of change in systolic arterial pressure (SAP) in patients with a high (group H) and patients with a low (group L) sensory block.

SAP = systolic arterial pressure
*p < 0.05 with respect to baseline
†p < 0.001 with respect to baseline

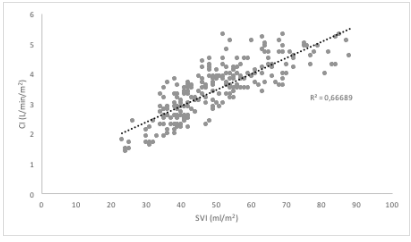

Figure 3: Scatter plot showing the correlation between the cardiac index (CI) and SVI values. The solid line represents the linear regression line.

R2 = measure of goodness-of-fit of linear regression

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