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Continuous Invasive Blood Pressure and Cardiac Output Monitoring during Cesarean Delivery

A Randomized, Double-blind Comparison of Low-dose versus *High-dose Spinal Anesthesia with Intravenous Phenylephrine or Placebo Infusion*

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Background: **Prevention of hemodynamic instability during cesarean delivery during spinal anesthesia has been the aim of several studies. Noninvasive monitoring has been used in all previous studies. This is the first study in healthy pregnant women with continuous invasive recording of arterial blood pressure, cardiac output, and systemic vascular resistance. The aim of this randomized trial was to compare the effects of two different intrathecal doses of bupivacaine, with or without intravenous phenylephrine infusion, on cardiac output and systolic blood pressure.**

Methods: **In this double-blinded study, 80 healthy women scheduled to undergo elective cesarean delivery were randomly assigned to one of four different groups receiving 7 mg spinal bupivacaine with or without a concomitant low-dose infusion of phenylephrine (0.25 $\mu g \cdot kg^{-1} \cdot min^{-1}$) or 10 mg spinal bupivacaine with or without phenylephrine infusion. All patients had 4 μg sufentanil added to the spinal solution and had cohydration with 750 ml saline, 0.9%.**

Results: **The low-dose spinal bupivacaine group with intravenous phenylephrine infusion was the most stable group regarding all hemodynamic variables. The authors found significant differences between this group and the group that was given the high dose of bupivacaine with intravenous placebo infusion regarding cardiac output ($P = 0.005$), systemic vascular resistance ($P < 0.0001$), and systolic blood pressure ($P = 0.012$).**

Conclusions: **This study shows that low-dose bupivacaine (with sufentanil), combined with a low-dose infusion of phenylephrine and moderate cohydration, gives the best hemodynamic stability during spinal anesthesia for cesarean delivery.**

HYPOTENSION after subarachnoid block for cesarean delivery is common, and several different interventions for the prevention of hypotension have been investigated.[1] Cyna *et al.*[1] concluded in the last Cochrane Review that no single method completely prevents hypotension during cesarean delivery. Most of the studies use a high dose of local anesthetic in the spinal solution, which may be the main cause of hypotension. Previous studies[2,3] have shown that reducing the dose reduces the incidence of hypotension. In 2005, Ngan Kee *et al.*[4] published a study that seemed to have solved the problem with only 1.9% hypotension. They used high doses of intravenous phenylephrine and a high volume of cohydration. The aim of the anesthetic regimen chosen should be to preserve hemodynamic stability of the patients, including uterine blood flow. All previous studies have used noninvasive hemodynamic monitoring, typically measuring blood pressure every minute or even less frequently. Invasive monitoring gives continuous measurements of blood pressure, systemic vascular resistance (SVR), and cardiac output (CO) and may increase our understanding of hemodynamic changes during spinal anesthesia and cesarean delivery.

The aims of this randomized controlled trial were to compare the effects of two different doses of bupivacaine for spinal anesthesia and the effects of prophylactic intravenous phenylephrine infusion compared with placebo on hemodynamic variables measured with invasive methods.

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Materials and Methods

The Ethical Committee of Southern Norway (Oslo, Norway) and the Norwegian Medicines Agency (Oslo, Norway) approved the study protocol. Healthy pregnant women at term with a singleton pregnancy scheduled to undergo elective cesarean delivery between August 2005 and April 2007 at the Birth Clinic, Rikshospitalet University Hospital (Oslo, Norway), were asked to participate. Patients were not eligible if they had preexisting or gestational hypertension, preeclampsia, cardiovascular or cerebrovascular disease, a height less than 160 cm or greater than 180 cm, prepregnancy body mass index greater than 32 kg/m^2, or contraindications to spinal anesthesia. All subjects gave written consent after oral and written information. One hundred twenty-nine women were asked to participate, 17 did not consent, and 32 were excluded for various reasons (fig. 1). The

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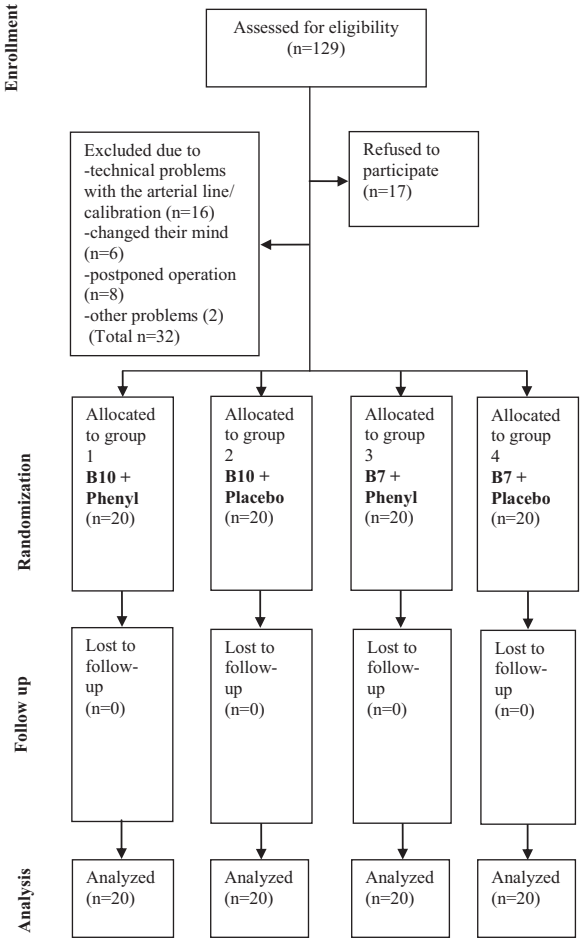

Fig. 1. Flow diagram of the trial procedure.

remaining 80 women were randomly assigned to one of the four treatment groups and included in the analyses.

This was a prospective, randomized, double-blind, parallel-group, placebo-controlled study comparing the hemodynamic effects of a high dose of spinal anesthesia with isobaric bupivacaine 10 mg (B10) with a low dose of 7 mg (B7), and the prophylactic effect of 0.25 $\mu g \cdot kg^{-1} \cdot min^{-1}$ intravenous phenylephrine infusion (Phenyl) with placebo. Group 1 (B10/Phenyl) received spinal anesthesia with 10 mg isobaric bupivacaine, 4 μg sufentanil, and 0.9% saline to a total volume of 3 ml, and a phenylephrine infusion of 0.25 $\mu g \cdot kg^{-1} \cdot min^{-1}$ intravenously. Group 2 (B10/Placebo) had the same spinal anesthesia as group 1 and placebo infusion intravenously. Group 3 (B7/Phenyl) received spinal anesthesia with 7 mg isobaric bupivacaine, 4 μg sufentanil, and 0.9% saline to a total volume of 3 ml, and a phenylephrine infusion of 0.25 $\mu g \cdot kg^{-1} \cdot min^{-1}$ intravenously. Group 4 (B7/Placebo) had the same spinal anesthesia as group 3 and placebo infusion intravenously.

The primary outcome measures were group differences in systolic blood pressure (SBP) and CO. Secondary outcomes were group differences in SVR, mean arterial pressure, diastolic blood pressure, stroke volume, heart rate, duration of motor block, nausea, and umbilical cord pH and base excess. In addition, we registered body mass index, sensory block, Apgar score at 1 and 5 min, operation time, induction time, and pruritus. Side effects were registered in all patients who were included, and an intention-to-treat analysis was performed.

The senior author, who was not involved in the handling of the drugs or the participants, performed the randomization in blocks of eight to four groups of equal size using a list of random numbers according to the Moses-Oakford algorithm.[5] Block size and randomization codes were not revealed to the investigators until all measurements and calculations had been entered into the database. To maintain blinding of both patients and examiner throughout the study, syringes for each patient were prepared in the morning of surgery by a doctor or nurse not involved in the treatment or assessment of the patients. The test drugs were prepared according to information in opaque, sealed envelopes marked with a randomization number only. A 50-ml syringe containing 30 ml phenylephrine or placebo, and a 10-ml syringe containing the spinal solution marked with the randomization number and neutral study information were delivered to the primary investigator in the operating theater. Unblinding of the investigators was tested by registering a guess at the treatment combination just after induction of spinal anesthesia and a second guess when the intravenous test drugs were stopped after 20 min.

The patients had no premedication or prehydration but were allowed to drink clear liquids up to 2 h before surgery. An 18-gauge intravenous cannula was inserted in each forearm. A 20-gauge arterial line was inserted in the radial artery after local skin infiltration with lidocaine. Standard monitoring with electrocardiography and pulse oximetry were attached. The LiDCO*plus* (LiDCO Ltd., Cambridge, United Kingdom) is a monitor providing continuous hemodynamic measurements. This new minimally invasive technique is based on two methods: a continuous arterial waveform analysis system (PulseCO) coupled to a single-point lithium indicator dilution calibration system (LiDCO). For the calibration (measuring actual CO), 0.3 mmol lithium chloride is injected through a peripheral line, and the lithium is detected by an external lithium ion–sensitive external electrode connected to a peripheral arterial line. The lithium dose has no pharmacologic effect on the woman or the fetus.[6] The LiDCOPlus gives continuous blood pressure and a beat-to-beat measurement of CO, stroke volume, and SVR.[7,8]

Baseline measurements of hemodynamic variables in each patient were performed after calibration of CO. A 1-min mean value of every variable was calculated when the women had been lying supine with a wedge pillow beneath the right hip for 5 min.

With the patient in the right lateral position, spinal anesthesia was induced in the L2–L3 vertebra interspace

after skin infiltration with lidocaine. A Portex combination set (Portex, Smiths, United Kingdom) with an 18-gauge epidural needle and a 27-gauge pencil-point spinal needle was used for a combined spinal–epidural with a needle-through-needle technique. Three milliliters of the blinded spinal test drug solution (7 or 10 mg bupivacaine and 4 μg sufentanil) was injected before inserting the epidural catheter 4 cm with the Tuohy needle opening facing cephalad. After securing the epidural catheter, the patient was turned back to the supine position with a wedge pillow under the right hip and a left lateral tilt of 15°. The upper sensory level of anesthesia was measured as loss of cold sensation (using alcohol 70% with chlorhexidine) and loss of tactile sensation (using a 50-g von Frey filament, No. 18, Aesthesiometer; Somedic, Hörby, Sweden) after 5 min. Failure to reach cold upper sensory level T8 was treated with epidural injection of 8 ml chloroprocaine, 30 mg/ml. Motor block duration was defined as the time from the induction of spinal anesthesia until the patient was able to perform a bilateral straight leg lift.

All of the women had a rapid infusion of 0.9% saline, 750 ml intravenously, when spinal anesthesia was induced. At the same time, the intravenous phenylephrine or the placebo infusion was started at 0.25 $\mu g \cdot kg^{-1} \cdot min^{-1}$ using a syringe pump (IVAC P7000; Alaris, Basingstoke, United Kingdom). The intravenous infusion was ended after 20 min. Hypotension was defined as SBP less than 90 mmHg. A bolus of 30 μg intravenous phenylephrine was given as rescue medication when SBP was less than 90 mmHg. If hypotension was combined with bradycardia (heart rate $<$ 55 beats/min), a bolus of 5 mg ephedrine was given. According to our protocol, the phenylephrine or placebo infusion would be stopped if mean arterial blood pressure was greater than 120 mmHg. Oxygen was not routinely given unless the arterial oxyhemoglobin saturation decreased to less than 95% (pulse oximeter).

After delivery, 5 U oxytocin was injected as an intravenous bolus. Arterial and venous blood samples (pH, base excess, partial pressure of carbon dioxide, partial pressure of oxygen) were taken from the umbilical cord and analyzed with a Radiometer ABL 800 analyzer (Radiometer A/S, Copenhagen, Denmark). Apgar scores after 1 and 5 min were recorded by the midwife.

Statistical Analysis

The main outcomes of this trial were SBP and CO after spinal anesthesia. With an SD of CO of 1.1 l/min (obtained from a pilot study), we needed to include 20 patients in each group to show a mean difference in CO of 1 l/min with 80% power and a significance level of 5% (SamplePower; SPSS, Chicago, IL).

We considered 15 mmHg as a clinically interesting mean difference in SBP between the groups. With an SD of 12.9 mmHg (obtained from a pilot study), we needed to include 17 patients in each group to show a mean difference in SBP of 15 mmHg with 80% power and a significance level of 5%.

The hemodynamic data were stored in the LiDCO*plus* monitor and downloaded as .csv files (text files) for each patient when the patient was discharged from the postoperative unit 2 h after surgery. Construction of the data set was performed using MatLab version R2007a (The MathWorks, Natick, MA). The beat-to-beat data set was transformed into average values every 10 s. Outliers, defined as extreme values and values more than 30% different from the two previous values, were considered erroneous and omitted from the data set. All data were constructed before breaking the randomization codes to ensure against biased handling of the data.

We used the linear mixed model in SPSS to analyze the changes in hemodynamic variables as a function of time in the four study groups. SPSS statistical program version 15.0 was used for analysis of all of the data. Treatment groups and time are treated as fixed factors, and baseline values are treated as a covariate. Use of rescue phenylephrine is included as a covariate in the analysis because we did not correct for use of rescue phenylephrine in the raw data. The same analysis was applied for the other variables as CO, SVR, mean arterial blood pressure, diastolic blood pressure, heart rate, and stroke volume. Normally distributed data are presented as mean and SD. Mean values with confidence intervals (CIs) for the 10-min period analyzed and mean maximum changes with CIs are presented for CO and SBP. Relative risks (RRs) for 20% and 30% reduction in SBP and RR for nausea are presented with CIs.

The shortest time from induction of spinal anesthesia to delivery was 11 min. The beat-to-beat data set obtained during the first minute contains a lot of disturbance because the patients were changing from the right lateral to the supine position. For this reason, and before breaking the randomization code, we decided to omit the first minute from the statistical analysis of the data from the first 11 min after spinal anesthesia.

Results

The patient flow diagram is illustrated in figure 1. Patients' characteristics (table 1) and baseline hemodynamic variables (table 2) in the four groups were similar. The group differences in CO and SBP were statistically significant ($P = 0.033$ and $P = 0.049$, respectively; table 3). Subsequent pairwise comparisons revealed that group 3 (B7/Phenyl), given spinal anesthesia with 7 mg bupivacaine in combination with a prophylactic intravenous phenylephrine infusion at 0.25 $\mu g \cdot kg^{-1} \cdot min^{-1}$, had significantly less hemodynamic changes compared with the other groups. These differences were most pronounced in the comparison between group 3 (B7/Phenyl) and group 2 (B10/Placebo), given spinal anesthesia

Table 1. Patient Characteristics and Time

	B10/Phenyl, n = 20	B10/Placebo, n = 20	B7/Phenyl, n = 20	B7/Placebo, n = 20	*P* Value
Indtime, min	18 (1)	17 (1)	18 (1)	18 (1)	0.608
Surgery, min	33 (3)	29 (1)	33 (3)	33 (3)	0.573
Age, y	34 (1)	35 (1)	34 (1)	34 (1)	0.958
GA, wk	38.5 (0.8)	38.5 (1.0)	38.3 (0.9)	38.8 (0.8)	0.261
Weight, kg	80.5 (2.4)	79.3 (2.5)	81.1 (1.9)	81.1 (2.7)	0.945
Height, m	1.70 (0.01)	1.69 (0.01)	1.69 (0.01)	1.69 (0.01)	0.707
BMI, kg/m^2	27.7 (0.8)	27.8 (0.8)	28.7 (0.8)	28.3 (1.0)	0.839
BMIpre, kg/m^2	22.6 (0.7)	22.6 (0.8)	23.5 (0.7)	23.1 (0.8)	0.834

Data are presented as mean (SEM).

BMI = body mass index; BMIpre = prepregnancy body mass index; GA = gestational age; Indtime = induction time (time from spinal anesthesia to delivery).

with 10 mg bupivacaine and intravenous placebo infusion. The mean CO and SBP for the period analyzed were 7.6 l/min (95% CI, 7.0–8.3 l/min) and 118 mmHg (95% CI, 112–124 mmHg) for group 2 (B10/Placebo), compared with 6.3 l/min (95% CI, 5.6–6.9 l/min) and 130 mmHg (95% CI, 123–136 mmHg) for group 3 (B7/Phenyl). The hemodynamic changes are shown in figure 2. Looking at CO, the figure shows that all four groups had a prominent increase. Group 2 (B10/Placebo) had a mean maximum increase of 59.7% (95% CI, 38.5–80.9%) from baseline, compared with a 32.8% increase (95%CI 20.8–44.9) in group 3 (B7/Phenyl). Looking at SBP, the figure shows that all four groups had a similar decrease in the first minutes. Then the group differences became prominent, with a mean decrease of 32.1% (95% CI, 25.6–38.6%) from baseline in group 2 (B10/Placebo) and a mean decrease of 16.8% (95% CI, 9.8–23.7%) in group 3 (B7/Phenyl) (table 4). RRs for 20% and 30% reduction in SBP between the two most different groups, 2 (B10/Placebo) and 3 (B7/Phenyl), were 2.5 (95% CI, 1.2–5.2) and 3.7 (95% CI, 1.2–11.3), respectively. RR for nausea between groups 2 and 3 was 4.3 (95% CI, 1.4–12.9). The numbers of patients given a rescue vasoactive drug, phenylephrine or ephedrine, because of clinically significant hypotension (SBP $<$ 90 mmHg) were not statistically significant different between the treatment groups (table 5).

Comparing the phenylephrine groups (groups 1 and 3) with the placebo groups (groups 2 and 4), we found statistically significantly lower CO ($P = 0.009$) and heart rate ($P = 0.004$) but not SBP ($P = 0.331$) (fig. 3).

Comparing the high-dose bupivacaine groups (groups 1 and 2) with the low-dose bupivacaine groups (groups 3 and 4), we found statistically significant differences in SBP ($P = 0.009$) but not in CO ($P = 0.186$). RRs for 20% and 30% reduction in SBP between the high-dose groups and the low-dose groups were 1.6 (95% CI, 1.1–2.4) and 2.1 (95% CI, 1.4–4.1), respectively. RR for nausea was 2.4 (95% CI, 1.2–4.9).

There was a statistically significant difference between the four treatment groups in mean umbilical artery and vein base excess (table 6). The umbilical artery base excess was lower in the high-dose bupivacaine groups compared with the low-dose bupivacaine groups ($P = 0.003$), whereas the corresponding difference in umbilical artery pH did not reach statistical significance ($P = 0.09$). There were missing blood samples from 15 umbilical cords.

We found no group difference in maximum sensory block height at 5 min ($P = 0.354$ for cold and $P = 0.183$ for tactile sensation). Motor block duration was 99 min (95% CI, 84–114 min) in the low-dose groups compared with 140 min (95% CI, 124–156 min) in the high-dose groups ($P < 0.0001$). One patient in the B10 groups (n = 40) and 3 patients in the B7 groups (n = 40) needed epidural supplementation with 30 mg/ml chloroprocaine, 8–20 ml. These patients were not included in analysis of the duration of motor block. No patients needed general anesthesia. Eleven patients (13.8%) had

Table 2. Baselines of Hemodynamic Variables

	B10/Phenyl, n = 20	B10/Placebo, n = 20	B7/Phenyl, n = 20	B7/Placebo, n = 20	*P* Value
CO, l/min	6.7 (0.3)	7.0 (0.4)	6.1 (0.3)	6.3 (0.3)	0.253
SVR, $dyne \cdot s \cdot cm^{-5}$	1,120 (74)	1,098 (66)	1,244 (94)	1,145 (70)	0.553
SBP, mmHg	140 (3)	139 (4)	137 (4)	139 (4)	0.960
MAP, mmHg	94 (3)	95 (2)	94 (3)	91 (3)	0.693
DBP, mmHg	70 (3)	72 (2)	71 (3)	67 (2)	0.384
HR, beats/min	85 (3)	90 (4)	83 (3)	84 (4)	0.524
SV, ml	80 (4)	79 (5)	74 (3)	79 (6)	0.817

Values are presented as mean (SEM).

CO = cardiac output; DBP = diastolic blood pressure; HR = heart rate; MAP = mean arterial blood pressure; SBP = systolic blood pressure; SV = stroke volume; SVR = systemic vascular resistance.

Table 3. Mean Differences (*P* Values) in Hemodynamic Variables in the Treatment Groups

	Group	Time	Group × Time	Rescue
SBP	0.049*	<0.0001	<0.0001	<0.0001
CO	0.033†	<0.0001	<0.0001	0.204
MAP	0.001	<0.0001	<0.0001	<0.0001
DBP	0.001	<0.0001	<0.0001	<0.0001
SVR	<0.0001	<0.0001	<0.469	0.046
HR	0.016	<0.0001	<0.0001	0.979
SV	0.154	<0.0001	<0.005	0.487

* Comparing groups 2 and 3, $P = 0.012$. † Comparing groups 2 and 3, $P = 0.005$. CO = cardiac output; DBP = diastolic blood pressure; HR = heart rate; MAP = mean arterial blood pressure; SBP = systolic blood pressure; SV = stroke volume; SVR = systemic vascular resistance.

no pruritus, 59 patients (73.8%) had little or moderate pruritus, and 9 patients (11.3%) had severe pruritus.

The investigators guessed the correct intervention of study group in only 22 of 80 patients after inducing spinal anesthesia and in 24 of 80 patients after finishing the phenylephrine or placebo infusion. This documents a successful blinding.

Discussion

This randomized controlled trial demonstrates that the hemodynamic instability due to spinal anesthesia during cesarean delivery under spinal anesthesia can be reduced by decreasing the intrathecal dose from 10 mg to 7 mg bupivacaine. We also document a significant effect of a continuous infusion of low-dose phenylephrine ($0.25\ \mu g \cdot kg^{-1} \cdot min^{-1}$) compared with placebo. The patient group given low-dose spinal anesthesia and prophylactic phenylephrine (B7/Phenyl) had the least changes from baseline hemodynamic variables (fig. 2), and all of the hemodynamic variables were statistically significantly different compared with the high-dose group (B10/Placebo) receiving 10 mg bupivacaine and

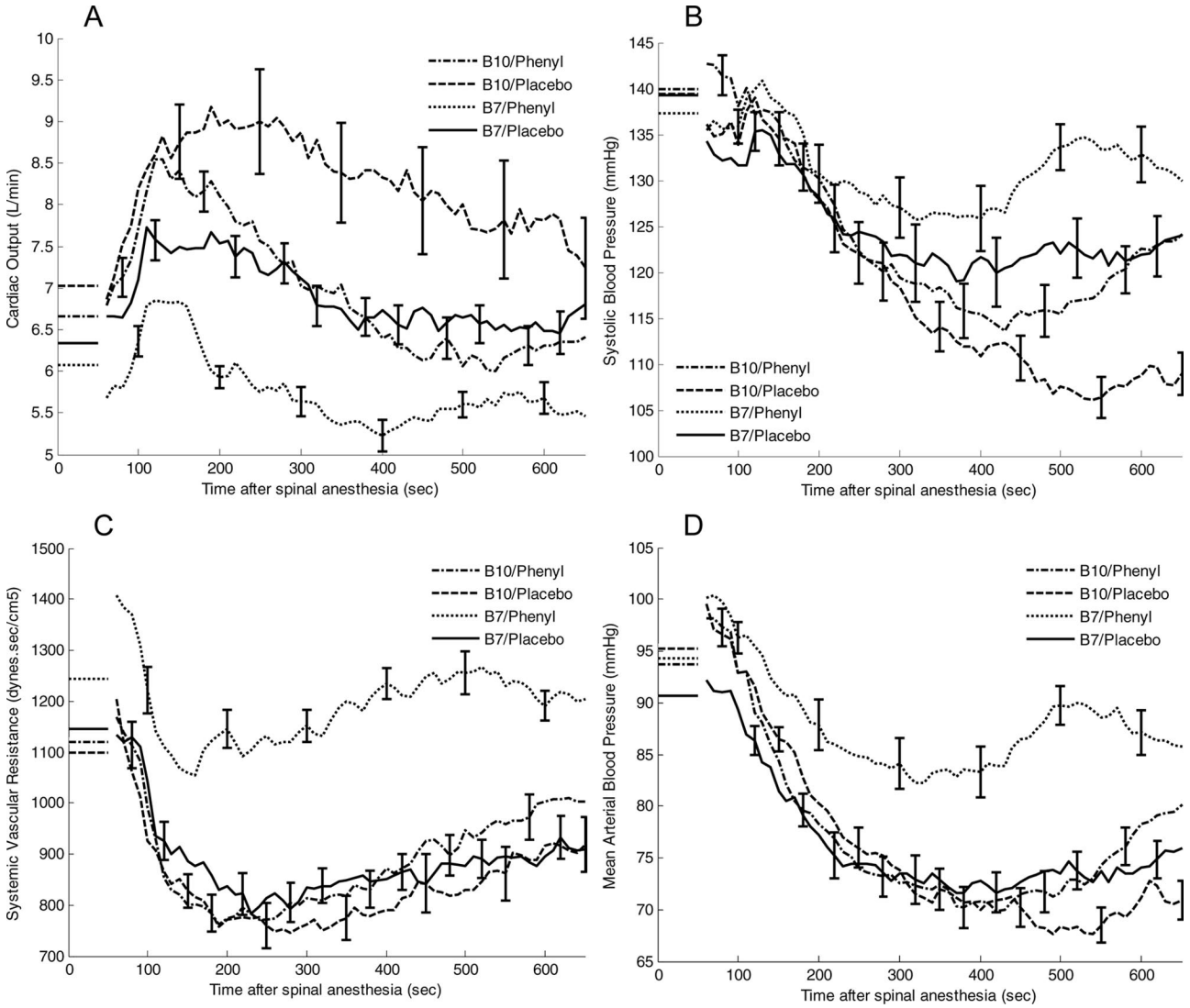

Fig. 2. Mean differences in hemodynamic variables between the four treatment groups. (*A*) Cardiac output. (*B*) Systolic blood pressure. (*C*) Systemic vascular resistance. (*D*) Mean arterial pressure. Baseline is marked on the y label. SE for each group is marked as error bars.

Table 4. Maximum Changes in Cardiac Output and Systolic Blood Pressure

	B10/Phenyl, n = 20	B10/Placebo, n = 20	B7/Phenyl, n = 20	B7/Placebo, n = 20
CO, l/min				
Maximum	9.6 (8.7–10.6)	11.6 (8.8–14.4)	7.8 (7.3–8.3)	9.5 (8.4–10.6)
Change, l/min	3.0 (2.5–3.5)	4.6 (2.5–6.7)	1.7 (1.2–2.3)	3.2 (2.5–3.9)
% Change	45.2 (36.4–54.0)	59.7 (38.5–80.9)	32.8 (20.8–44.9)	51.5 (40.7–62.2)
Time, s	192 (142–242)	256 (177–335)	164 (111–216)	302 (201–402)
SBP, mmHg				
Minimum	101 (91–111)	94 (85–103)	114 (103–125)	103 (92–114)
Change, mmHg	39 (28–50)	45 (35–56)	24 (13–34)	37 (28–46)
% Change	27.5 (20.2–34.9)	32.1 (25.6–38.6)	16.8 (9.8–23.7)	26.6 (20.1–33.2)
Time, s	386 (297–475)	487 (416–558)	251 (157–344)	398 (302–493)

Values are presented as mean (95% confidence interval).

% Change = percentage change from baseline; CO = cardiac output; Maximum = mean maximum values in cardiac output; Minimum = mean minimum values in systolic blood pressure; SBP = systolic blood pressure; Time = time from spinal anesthesia to highest cardiac output or lowest systolic blood pressure.

placebo infusion. We found statistically significant differences in all hemodynamic variables except stroke volume between the four treatment groups. The hemodynamic curves showed an initial prominent decrease in SVR, and a concomitant increase in CO in all patients with a peak effect after approximately 3 min in the phenylephrine groups. In our study, the prophylactic phenylephrine infusion was started simultaneously with the intrathecal injection. To prevent the immediate hemodynamic changes, an additional initial bolus of phenylephrine at induction of spinal anesthesia may be a better approach. This can reduce the number of patients with clinically significant hypotension, reduce the need for rescue pressor drugs, and reduce hemodynamic instability.

A few previous studies of hypotension during cesarean delivery have focused on the intrathecal doses of local anesthetics. Ben-David *et al.*[2] compared 10 mg with 5 mg hypobaric bupivacaine and 25 μg fentanyl and showed that the low dose resulted in less hypotension, vasopressor requirement, and nausea. In a randomized controlled trial comparing 9.5 and 6.5 mg hyperbaric bupivacaine, van de Velde *et al.*[3] showed that the incidence of hypotension and the number of patients requiring rescue pressor were significantly reduced in the low-dose group. In a recently published study, the authors found no differences in noninvasively measured SBP between 12 and 4.5 mg hyperbaric bupivacaine.[9]

In the current study, we found statistically significant group differences for several primary and secondary outcome measures. The use of invasive monitoring made it possible to detect the immediate hemodynamic changes after spinal anesthesia. The vasodilatory effect of spinal anesthesia is expected, but the immediate effect on SVR and CO has not been shown before. These changes are of clinical relevance regarding regional anesthesia to pregnant women at risk (*i.e.*, cardiac disease) where prominent hemodynamic changes could be harmful and should be prevented.

Table 5. Distribution of Rescue Pressor Drugs

	B10/Phenyl, n = 20	B10/Placebo, n = 20	B7/Phenyl, n = 20	B7/Placebo, n = 20
Phenylephrine	8	11	4	8
Ephedrine	3	6	4	2

Data are presented as number of patients in each treatment group. One patient (group 3) received ephedrine only. All other patients were given phenylephrine first, before ephedrine.

We found that spinal anesthesia with 10 mg bupivacaine increases the risk of hypotension with an RR of 1.6 for 20% reduction of baseline SBP and an RR of 2.1 for 30% reduction of baseline SBP.

The risk of perioperative nausea, induced by hypotension, was also significantly higher in the groups given 10 mg bupivacaine compared with 7 mg (RR = 2.4). Three of 40 patients (7.5%) in the 7-mg bupivacaine group and 1 of 40 patients (2.5%) in the 10-mg group needed an epidural top-up. This trial was not powered to test whether this difference was of statistical significance. Using a combined spinal–epidural technique may be advisable when giving lower doses of bupivacaine for spinal anesthesia.

The efficacy and safety of prophylactic phenylephrine infusion during cesarean delivery has been thoroughly investigated.[4,10–12] We gave lower doses of phenylephrine than were used in a randomized controlled trial by Ngan Kee *et al.*[4] They found only 1.9% hypotension (defined as SBP < 80% of baseline), but 47% had reactive hypertension (defined as SBP > 120% of baseline). None of the patients in our trial had reactive hypertension. Our data show that there was a statistically significant lower heart rate and CO in the phenylephrine groups compared with the placebo groups, but all groups had an increase in heart rate and CO the first minutes (fig. 3). There was no statistically significant difference regarding stroke volume. Phenylephrine is an α_1 agonist that increases the blood pressure by increasing SVR. In addition, phenylephrine has a direct inotropic effect on the heart.[13] The fact that the phenylephrine groups had lower heart rate and CO than the placebo groups can be

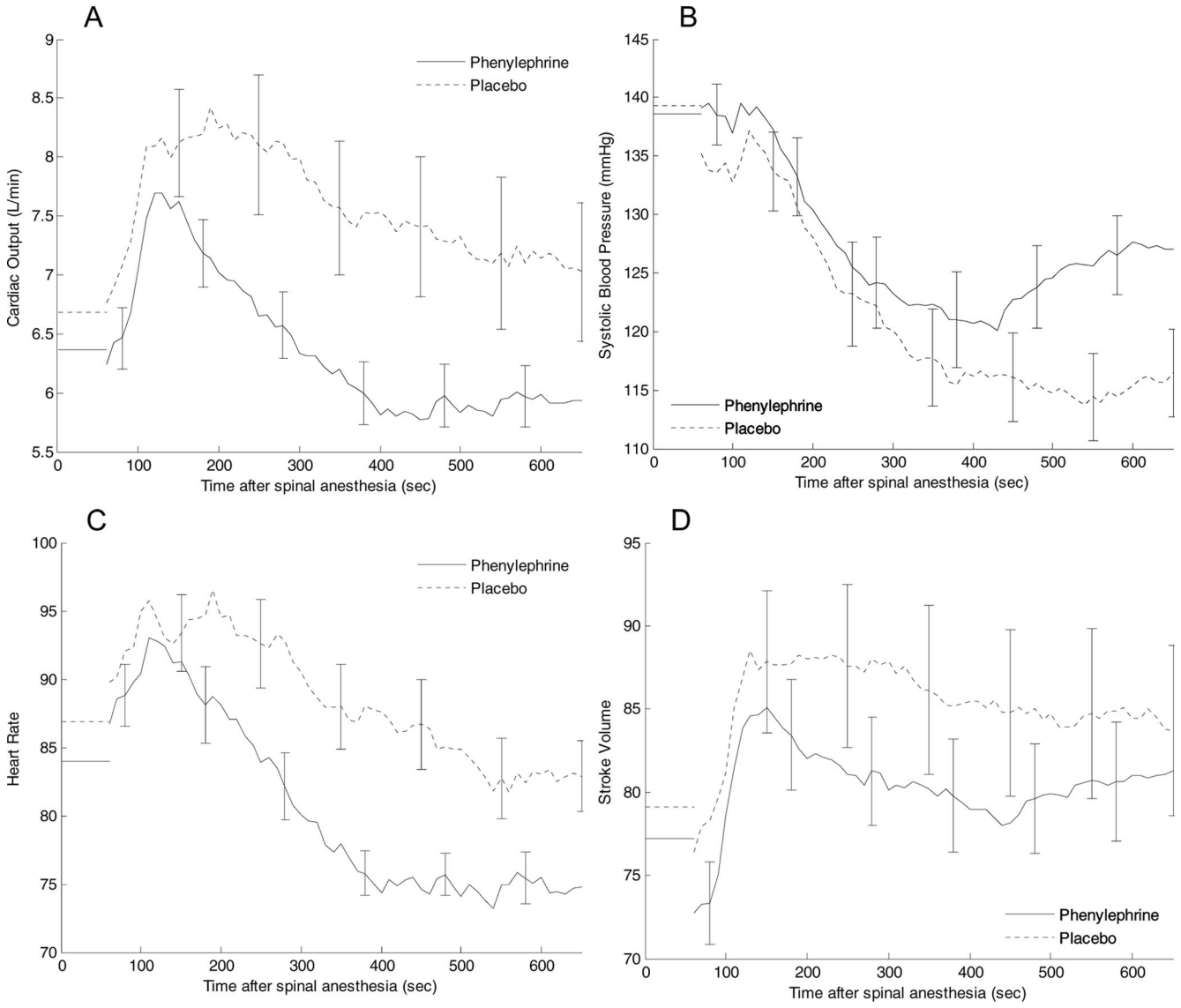

Fig. 3. Mean differences in hemodynamic variables between the phenylephrine groups and the placebo groups the first 11 min after spinal anesthesia. (*A*) Cardiac output. (*B*) Systolic blood pressure. (*C*) Heart rate. (*D*) Stroke volume. Baseline is marked on the y label. SE for each group is marked as error bars.

explained by the arterioconstrictive effect of phenylephrine resulting in high SVR and therefore a simultaneous reduction of cardiac output. The approach of keeping the blood pressure at baseline by infusing high doses of phenylephrine might be questioned in daily clinically practice because of a negative effect on CO. Allowing 10–20% decrease in blood pressure, reducing the doses of bupivacaine, and thereby reducing the need for phenylephrine may be a better approach for hemodynamic stability during cesarean delivery.

The baseline values of hemodynamic variables measured in this study are in the same range as findings published by Clark *et al.*[14] using Swan-Ganz in 10 healthy pregnant women at gestational age 36–38 weeks. The LiDCO*plus* system has never been used systematically in healthy pregnant women. The use of LiDCO*plus* has been validated in other patient groups,[15] but little has been published regarding its use in pregnant women.[16,17] This monitoring system, which is based on a pulse power analysis of the arterial blood pressure, gives reliable information about the rapid short-lasting changes in SBP, CO, and SVR after spinal anesthesia.

In conclusion, this study shows that low-dose bupivacaine (with sufentanil) combined with a low-dose infusion of phenylephrine and moderate cohydration, gives the best hemodynamic stability during spinal anesthesia for cesarean delivery. This study supports the view that prophylactic phenylephrine infusion should be part of standard clinical practice during spinal anesthesia for cesarean delivery.

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Table 6. Characteristics of the Newborn

	B10/Phenyl, n = 20	B10/Placebo, n = 20	B7/Phenyl, n = 20	B7/Placebo, n = 20	*P* Value
Birth weight	3,514 (109)	3,484 (106)	3,483 (138)	3,457 (72)	0.964
Apgar 1 < 7	1	0	0	2	
Apgar 5 < 7	0	0	0	0	
UA					
pH	7.26 (0.01)	7.27 (0.02)	7.29 (0.01)	7.29 (0.02)	0.400
BE	−2.3 (0.6)	−3.0 (0.5)	−0.7 (0.4)	−1.4 (0.7)	0.039
P_{CO_2}	7.4 (0.3)	6.9 (0.3)	7.3 (0.2)	7.1 (0.3)	0.635
P_{O_2}	1.8 (0.1)	1.7 (0.2)	2.2 (0.1)	2.2 (0.2)	0.042
UV					
pH	7.33 (0.01)	7.33 (0.02)	7.35 (0.01)	7.33 (0.02)	0.515
BE	−2.3 (0.4)	−3.3 (0.5)	−1.3 (0.3)	−1.4 (0.6)	0.011
P_{CO_2}	6.1 (0.3)	5.5 (0.3)	5.8 (0.2)	6.1 (0.2)	0.258
P_{O_2}	3.2 (0.29	3.0 (0.39	3.6 (0.2)	3.0 (0.2)	0.120

Values are presented as mean (SEM). Apgar 1 and Apgar 5 are scored 1 and 5 min after delivery.

BE = base excess; P_{CO_2} = partial pressure of carbon dioxide; P_{O_2} = partial pressure of oxygen; UA = umbilical artery; UV = umbilical vein.

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