Low-dose versus a Higher-dose Bupivacaine Spinal Anesthesia for Cesarean Delivery

To the Editor—We read with interest the article by Langesæter et al. 1 that investigated the hemodynamic effects of a low-dose versus a higher-dose bupivacaine spinal anesthesia for cesarean delivery. While the LiDCOplus (LiDCO Ltd., Cambridge, United Kingdom) monitor for continuous hemodynamic measurements seems promising because of its minimal invasiveness, the use of low-dose bupivacaine for spinal anesthesia during cesarean delivery poses several practical questions.

First, we would like to remark that among the various methods studied while incurring less frequent hypotension during cesarean delivery with spinal anesthesia, the only technique to date that has been shown to be effective is the combination of high-dose phenylephrine and crystalloid cohydration.

Our primary concern regarding the study by Langesæter et al. 1 is the high incidence (7.5%) of incomplete spinal block encountered with the low-dose local anesthetic. Also, we wonder why the upper target sensory level was T8 and not T4-5, and what the actually recorded upper sensory level of the block with both doses of spinal anesthesia was.

In addition, from a practical and safety point of view, it seems illogical to administer prophylactic phenylephrine with a systolic blood pressure of 140 mmHg.

The concern that the hemodynamic instability might come on the account of the quality of anesthesia is further emphasized by Ben David et al., 3 who found that with low-dose bupivacaine plus fentanyl, 8 out of 16 patients noted transient pain or pressure with stretching of the incision and/or with uterine fundal pressure at delivery.

We believe that a low-dose spinal anesthesia for cesarean delivery should only be employed with the combined spinal-epidural approach where epidural supplementation is feasible (as it was done in the present study). However, such an epidural supplementation may lead to hemodynamic instability by itself. If spinal anesthesia has to be supplemented with epidural local anesthetics, then a rapid-onset local anesthetics such as lidocaine is the preferable option.

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References

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In Reply—We thank Ngan Kee and Khaw for their response to our study 1 concerning invasive hemodynamic monitoring during spinal anesthesia for C-section. Some of the apparent disagreements seem to depend on the misinterpretation that we recommend a clinical practice identical with the strict study algorithm used in an experimental study.

We do not recommend an arterial line as routine in healthy parturients undergoing C-section. This was a study conducted to investigate the maternal hemodynamic changes induced by different variants of spinal anesthesia with the use of invasive monitoring. By using continuous invasive monitoring, we showed the immediate and prominent hemodynamic changes associated with spinal anesthesia in this patient group. This study documented that cardiac output increases—not decreases—after spinal anesthesia, which is contrary to previous assumptions published regarding the effects of spinal anesthesia. 2 This is the first study describing continuous invasive monitoring in healthy pregnant women during spinal anesthesia for C-section. Spinal anesthesia has theoretically been assumed to decrease cardiac output based on the reflex bradycardia induced by reduced preload on the cardiovascular receptors in the vena cava, right atrium, and left ventricle. The vasodilatory effect of sympathectomy has been thought to be moderate. Our study demonstrated a large decrease in systemic vascular resistance, and also that the changes were immediate within less than 3 min. To counteract these prominent and immediate changes, vasoconstrictor can be given prophylactically, and the logic choice of vasoconstrictor is an α-agonist, which counteracts the vasodilatory effect. Ephedrine, which mainly acts as a β-agonist, would further increase cardiac output. Ngan Kee and Khaw misinterpret us when they say we suggest to delay or withhold administration of phenylephrine to permit a decrease in blood pressure below baseline. On the contrary, we recommend starting phenylephrine prophylactically simultaneously with the spinal anesthesia, as we did in our study. In clinical practice, we also suggest giving a bolus of phenylephrine at start, in addition to the infusion, to further reduce the rapid hemodynamic changes observed in our study. Thus, the recommendation by Ngan Kee et al. 3–5 of prophylactic phenylephrine infusion during spinal anesthesia for C-section is supported by our article. When we designed our study, we did not know that we would demonstrate such immediate hemodynamic changes in less than 3 min. If we were to conduct this study today, we would have included a start bolus of phenylephrine, based on these findings.

In our study, a bolus of phenylephrine 30 μg IV was given as rescue medication when systolic blood pressure was below 90 mmHg. Ngan Kee and Khaw compare our invasive beat-to-beat blood pressure recordings with their results obtained by noninvasive intermittent blood pressure measurement. 3 We do not think such direct comparison is justified. In their study, 96% of patients had one or more intermittent measurements below their target of 80% of baseline systolic blood pressure, with accompanying nausea and vomiting in 40%. Obviously, their low-height patients receiving a large dose of spinal bupivacaine had considerably more prominent hemodynamic instability, as compared with our study patients. In our group receiving low-dose bupivacaine and low-dose phenylephrine, the mean maximum decrease in systolic blood pressure was 17%, measured with a beat-to-beat technology. With an intermittent noninvasive technique, these changes might not have been detected.
The doses of phenylephrine used in our study are small, even when rescue boluses of phenylephrine are added to the infusion. Compared to the doses used in our study, the first 10 minutes (2.8 μg/kg, including rescue phenylephrine, a total of 3.5 μg/kg were given). Ngan Kee et al. used much higher doses (18.8 μg/kg, 22.4 μg/kg, and 17.1 μg/kg) in their studies. Ngan Kee et al. used noninvasive monitoring, and therefore heart rate must be used as a surrogate marker for cardiac output. In their studies, heart rate decreased after spinal anesthesia. All our patients had an initial increase in heart rate. Even the small doses of phenylephrine (2.8 μg/kg) used in our study had a negative effect on cardiac output. We do not argue that these effects are unsafe or detrimental in healthy women, but Ngan Kee et al. used up to nine times as high doses of phenylephrine to keep blood pressure at baseline, will probably induce a considerably larger dose-dependent decrease in cardiac output. Ngan Kee and Khaw conclude that they continue to advocate aggressive maintenance of blood pressure using phenylephrine, although the cardiac output is slightly less with this method. As phenylephrine has a dose-dependent effect on cardiac output, they cannot conclude that the effect on cardiac output using high doses in their studies is only minor. We have shown that hemodynamic stability can be achieved by reducing the spinal bupivacaine dose combined with a moderate phenylephrine infusion.

In our study all participants received doses of spinal anesthetic decided by group assignment, while in clinical practice the dose is tailored according to height, body mass index, clinical status, and so forth. We do not recommend low-dose spinal anesthesia as a single shot to unselected women, but to use a combined spinal-epidural technique. In our clinical practice we use low doses of bupivacaine administered with a single-shot spinal to selected women with a height of less than 165 cm, especially when combined with a high body-mass index. Our study included women with a height between 160 to 180 cm (mean height, 168 cm), as compared with a mean height of 157 cm in Ngan Kee et al.'s studies. This could explain the incidence of insufficient spinal anesthesia in three women in the low-dose group.

Based on our study, we have recommended to give spinal anesthesia in a more balanced way by giving lower doses of spinal bupivacaine, which will reduce the need of cohydration and phenylephrine to compensate for the induced hemodynamic instability.

We thank Raghunathan et al. for their interesting contribution on invasive monitoring devices. We have no experience with the Vigileo device (Edwards Lifesciences LLC, Irvine, CA). As the authors point out, rapid changes in pulsatility of the arterial system would not be reliable. As our study demonstrates, the hemodynamic changes after spinal anesthesia in cesarean patients are immediate, with a prominent decrease in systemic vascular resistance in less than 3 min, and this would probably not be correctly analyzed by the Vigileo device. This view is also supported in a review by de Waal et al., stating that "rapid changes in vascular motor tone lead to impaired accuracy of cardiac output monitoring," using the Vigileo device. The maximal hemodynamic changes after an IV bolus of 5 units oxytocin is detected after 30 to 40 s, and in less than 2 min the hemodynamic is normalized. Therefore, the conclusion by Dyer and James that the use of the Vigileo device may not be suitable in this setting seems reasonable.

We share Raghunathan et al.’s interest in possible use of stroke volume variation and pulse pressure variation measurements. The software of the LiDCCplus monitor (LIDCO Ltd., Cambridge, United Kingdom) was improved to include stroke volume variation and pulse pressure variation during the study period. We have data on stroke volume variation and pulse pressure variation on 35 of the 80 healthy parturients included in this study, and in approximately 100 other spontaneously breathing pregnant women with pre eclampsia or cardiac disease. The time schedule did not allow us to analyze these data to be commented on here, but we plan to look at our data and see if stroke volume variation and pulse pressure variation can give any valuable information on fluid responsiveness in spontaneously breathing patients.

We appreciate the comments from Evron and Ezri on our study. Three of 40 patients receiving low-dose and 1 of 40 patients receiving high-dose bupivacaine needed an epidural top-up because of incomplete spinal block. Our study was not designed to look at any statistically significant differences between the groups regarding incomplete spinal block. The upper sensory level was not a main outcome in our study. We tested the sensory level after 5 min with cold and pin prick. If the sensory level was T8 or lower after 5 min, the patients were given an epidural top-up. We chose to design our study as close to clinical practice as possible. To shorten the induction time (time from spinal anesthesia to delivery) is a main focus in our department. If we had tested sensory level after 10 or 15 min, we might have avoided any epidural top-up, but then the surgery would be delayed. For the cold test, the mean upper sensory level was the same in the low-dose groups as in the high-dose groups: T3 (C7-T8). For the pinprick test, the mean upper sensory level was T5 (T2-T12) in the high-dose groups, and T6 (T1-T11) in the low-dose groups. All our patients were given the same volume of 3 ml spinal solution, which included 4 μg (0.8 ml) sufentanil.

The authors refer to a study by Ben David et al., comparing 5 mg bupivacaine and 25 μg fentanyl to 10 mg bupivacaine for spinal anesthesia. This small study showed 94% hypotension in the high-dose group, and 31% in the low-dose group. The low-dose bupivacaine provided surgical anesthesia in all their patients, and all patients reported a high level of satisfaction with the anesthesia, even though 8 of 16 patients had transient pain or pressure with stretching. In our clinical practice (but not in our study) we spread 20 ml lidocaine 1% on the peritoneum in case of discomfort as a result of stretching or pressure. Our experience is in agreement with Ben David et al. stating that patients are more distressed by the unpleasant sensation associated with hypotension and nausea than the transient pressure or stretching.

As we have replied to Ngan Kee and Khaw, we do not recommend in our article low-dose bupivacaine as a single-shot to unselected women. We recommend the use of a combined spinal-epidural technique when using low doses. However, in our daily practice we use low-dose spinal bupivacaine as a single shot in selected women, based on our clinical experience that shorter women, especially with a high body mass index, require lower spinal doses of bupivacaine.

Before conducting this study, we would agree that it may seem illogical to administer prophylactic phenylephrine with a baseline systolic blood pressure of 140 mmHg. We followed a study protocol based on randomization into four groups. We, the investigators, were blinded to the phenylephrine/placebo infusion. After analyzing the data and having the results of the study we think prophylactic phenylephrine infusion is mandatory to prevent hypotension, even with a high baseline blood pressure. This is because the hemodynamic changes induced by spinal anesthesia are immediate and prominent, with maximal changes in systemic vascular resistance and cardiac output in less than 3 min. Without any prophylactic phenylephrine, the hypotension cannot be prevented. In addition to a prophylactic phenylephrine infusion from start of spinal anesthesia, we also recommend an initial bolus of phenylephrine.

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In Reply—We would like to thank Kee et al. for their interesting comments. Regarding the placement of peripheral arterial catheters, we did not suggest their use in routine elective cases and agree that this is inappropriate outside the research setting. The incidence of complications from short-term arterial cannulation is vanishingly rare, and the placement of a 20-gauge arterial line would be regarded by many ethics committees as acceptable, provided the appropriate informed consent has been obtained and the clinical significance of the scientific issues addressed in the protocol justify it. In this regard, important research applications of noninvasive cardiac output monitoring are the illustration of the hemodynamic effects of spinal anesthesia and the effects of vasoactive drugs such as ephedrine, phenylephrine, and oxytocin.1–3 Of course in complicated cases of severe complications from short-term arterial cannulation is vanishingly rare, this is inappropriate outside the research setting. The incidence of nausea and vomiting, reductions in cardiac output may have far more serious consequences, particularly in cases of undiagnosed cardiac disease that occur in high-turnover, low-resource maternity units. It should also be remembered that the incidence of nausea and vomiting during spinal anesthesia for elective cesarean delivery varies considerably between populations. In our institution it is less than 10%. If maintenance of blood pressure is to be the predefined endpoint during spinal anesthesia, we believe it is best achieved by a combination of loading dose and continuous infusion, and not by continuous infusion alone, according to classic pharmacokinetic theory relating to achieving rapid changes in the plasma level of a drug. In the quoted article,5 it was shown that starting an infusion of phenylephrine when the blood pressure had decreased to 80% of baseline resulted in a greater incidence of nausea and vomiting than targeting a blood pressure of 100%. We agree that simply starting an infusion of phenylephrine at 80% of baseline blood pressure is likely to prolong the recovery from this pressure and may result in a longer period of hypotension, and this delay could result in nausea and vomiting. A bolus of phenylephrine before starting the infusion should obviate this problem, since the peak vasopressor effect is rapid when compared with ephedrine.

In addition, we think that the administration of a relatively high-dose prophylactic infusion of phenylephrine in every patient5 is likely to cause a significant incidence of hypertension and bradycardia (21 and 22%, respectively, in the quoted article). In our experience this equates to a reduction in cardiac output. Waiting for a moderate decrease in blood pressure and then using an immediate rapid phenylephrine bolus is likely to restore arterial pressure early with less risk of overshoot of blood pressure or a fall in cardiac output to below baseline value.

It is our opinion that the approach of Langseter et al.3 is reasonable. This article suggests that cardiac output may increase after afterload reduction because of spinal anesthesia, in which case simply using a low-dose phenylephrine infusion ab initio to restore baseline systemic vascular resistance, but not exceed it, seems appropriate. Once again, the administration of an early bolus of phenylephrine could have improved hemodynamic stability, given that a low infusion rate of phenylephrine was employed. We agree that valid comparisons can only be made by the authors between regimens actually used in the study.

One of the benefits of α-agonists is that the uterine artery in pregnancy is less responsive to their effects than in the nonpregnant state.9 This finding, together with the well-preserved cord gas values after high-dose phenylephrine,3 suggests that phenylephrine is effective in sustaining uterine blood flow during spinal anesthesia by its effects on uterine artery perfusion pressure. We agree that regional flow in the uterus and placenta is pressure-dependent, and recognize the importance of maintaining maternal blood pressure. The fact that uterine blood flow is in excess of the minimum for fetal demand should allow for a modest decrease in uterine artery pressure after spinal anesthesia without any adverse clinical effects.

We agree that titration to a predefined endpoint is convenient using phenylephrine during most elective cesarean deliveries under spinal anesthesia, but why not include heart rate as an endpoint? Bradycardia and hypertension after phenylephrine administration indicate depression of maternal cardiac output,7 while tachycardia and hypotension in response to spinal anesthesia often indicate a pronounced decrease in systemic vascular resistance and a partial compensatory increase in cardiac output.5 (Robert Dyer, F.C.A.(S.A.), Department of Anesthesia, University of Cape Town, Cape Town, South Africa, unpublished data). The latter scenario is amenable to a bolus of phenylephrine followed by an infusion. Precipitous bradycardia and hypotension in response to spinal anesthesia signal a marked decrease in cardiac output.9 In this setting anticholinergics and/or ephedrine are more appropriate, in conjunction with positioning the patient to minimize aortocaval compression. So maintenance of both the baseline heart rate and blood pressure in patients having elective cesarean delivery under spinal anesthesia makes the best sense, because blood pressure does not always reflect cardiac output, and heart rate is a more reliable predictor.

We would also like to thank Raghunathan et al. for their comments and informative description of the function of the FloTrac/Vigileo monitor (Edwards Lifesciences LLC, Irvine, CA). It must be said that we have no experience with this monitor, and our comments are based upon an appraisal of the literature. Raghunathan et al. state that the Vigileo system is useful in many settings, and that acceptable bias and limits of agreement are shown in many investigations when compared with thermodilution measurements. However, there are publications suggesting that at the limits of systemic vascular resistance, this monitor may be inaccurate. This may be important when attempting to measure rapid responses to vasoressors or vasodilators, either for research or clinical purposes.

For example, during liver transplantation, a recent study comparing thermodilution measurements employing a pulmonary artery catheter...