

5. Ngan Kee WD, Khaw KS, Ng FF, Lee BB: Prophylactic phenylephrine infusion for preventing hypotension during spinal anesthesia for cesarean delivery. *Anesth Analg* 2004; 98:815-21

6. Critchley LA, Critchley JA: A meta-analysis of studies using bias and precision statistics to compare cardiac output measurement techniques. *J Clin Monit Comput* 1999; 15:85-91

7. de Waal EEC, Wappler F, Buhre W: Cardiac output monitoring. *Curr Opin Anaesth* 2009; 22:71-7

8. Langesæter E, Rosseiland LA, Stubhaug A: Hemodynamic effects of oxytocin during cesarean delivery. *Int J Gynecol Obstet* 2006; 95:46-7

9. Dyer RA, James MF: Maternal hemodynamic monitoring in obstetric anesthesia. *ANESTHESIOLOGY* 2008; 109:765-7

10. De Backer D, Pinsky MR: Can one predict fluid responsiveness in spontaneously breathing patients? *Intensive Care Med* 2007; 33:1111-3

11. Ben-David B, Miller G, Gavriel R, Gurevitch A: Low-dose bupivacaine-fentanyl spinal anesthesia for cesarean delivery. *Reg Anesth Pain Med* 2000; 25:235-9

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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.<sup>1-3</sup> Of course in complicated cases of severe preeclampsia, arterial lines become a standard of care in most units. We also agree that arterial lines are not in general necessary for titration of phenylephrine infusions in routine cases. In inexperienced hands however, caution is required with a highly potent drug such as phenylephrine to avoid dosage and dilution errors.<sup>4</sup>

We agree that nausea and vomiting is an important endpoint, since limitation of these symptoms goes a long way towards making spinal anesthesia a pleasant and happy experience for mothers. However, not only is cardiac output an important endpoint, but it is our view that significant depression of maternal cardiac output because of the use of doses of phenylephrine causing hypertension and baroreceptor mediated bradycardia, is to be avoided. Although much less frequent than 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,<sup>5</sup> 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 patient<sup>5</sup> 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 Langesæter *et al.*<sup>3</sup> is reasonable. This article suggests that cardiac output may increase after after-load 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  $\alpha$ -agonists is that the uterine artery in pregnancy is less responsive to their effects than in the nonpregnant state.<sup>6</sup> This finding, together with the well-preserved cord gas values after high-dose phenylephrine,<sup>5</sup> 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,<sup>7</sup> 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,<sup>3</sup> (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.<sup>8</sup> 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 vasopressors or vasodilators, either for research or clinical purposes.

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

and the Vigileo system showed a bias of 1.3 l/min and 95% limits of agreement of  $-1.5$ – $4.1$  l/min.<sup>9</sup> The percentage error was 54%. Also, there was increased bias when systemic vascular resistance was low. In only 68% of readings did the direction of change agree between the two monitors. The view was expressed by the authors of this article that only 2 out of 13 published studies on the Vigileo system fulfill the recommended criteria; namely, that the combined agreement error should be  $<30\%$  for a new monitoring device to be accepted for clinical practice.<sup>10</sup>

In terms of response time, a study showing a decrease in cardiac output after phenylephrine administration as measured by continuous thermodilution, as compared with an increase using the Vigileo system, remains a concern.<sup>11</sup> Particularly in the setting of basic research in obstetric anesthesia, the measurement of rapid changes after the use of vasoactive agents contributes knowledge impacting on clinical management. The recalculation of the proportionality constant relating stroke volume to pulsatility in the Vigileo algorithm, as described in a lucid editorial<sup>12</sup> and by Raghunathan *et al.*, takes place every minute. Such a delay would be problematic if one was interested in a beat-by-beat depiction of hemodynamic changes in circumstances where systemic vascular resistance was changing rapidly. Indeed, the authors own comments that “waiting a few minutes for auto-recalibration and the recalculation of  $\kappa$  is appropriate before relying on Vigileo-reported measurements” totally supports our editorial view that this instrument “may not be suitable for the study of rapid hemodynamic changes associated with obstetric anesthesia.”

We agree that studying systolic pressure variation, pulse pressure variation, and stroke volume variation in spontaneously breathing patients could be of great clinical benefit in the future in the prediction of fluid responsiveness, should the algorithm and software of the particular cardiac output device allow it.

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## References

1. Dyer RA, James MF: Hemodynamic monitoring in obstetric anesthesia. *ANESTHESIOLOGY* 2008; 109:765–7
2. Dyer RA, Piercy JL, Reed AR, Lombard CJ, Schoeman LK, James MF: Hemodynamic changes associated with spinal anesthesia for cesarean delivery in severe preeclampsia. *ANESTHESIOLOGY* 2008; 108:802–11
3. Langesaeter E, Rosseland LA, Stubhaug A: 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. *ANESTHESIOLOGY* 2008; 109:856–63
4. Ngan Kee WD, Khaw KS: Vasopressors in obstetrics: What should we be using? *Curr Opin Anaesthesiol* 2006; 19:238–43
5. Ngan Kee WD, Khaw KS, Ng FF: Comparison of phenylephrine infusion regimens for maintaining maternal blood pressure during spinal anaesthesia for Cesarean section. *Br J Anaesth* 2004; 92:469–74
6. Magness RR, Rosenfeld CR: Systemic and uterine responses to alpha-adrenergic stimulation in pregnant and nonpregnant ewes. *Am J Obstet Gynecol* 1986; 155:897–904
7. Stewart A, Fernando R, McDonald S, Hignett R, Jones T, Columb M, Abdul-Kadir R: Dose-dependent effects of phenylephrine for elective cesarean section under spinal anaesthesia: Implications for the compromised fetus? *Int J Obstet Anesth* 2008; 17(S1):S9
8. Kinsella SM, Tuckey JP: Perioperative bradycardia and asystole: Relationship to vasovagal syncope and the Bezold-Jarisch reflex. *Br J Anaesth* 2001; 86:859–68
9. Biancofiore G, Critchley LA, Lee A, Bindi L, Bisa M, Esposito M, Meacci L, Mozzo R, DeSimone P, Urbani L, Filippini F: Evaluation of an uncalibrated arterial pulse contour cardiac output monitoring system in cirrhotic patients undergoing liver surgery. *Br J Anaesth* 2009; 102:47–54
10. Critchley LA, Critchley JA: A meta-analysis of studies using bias and precision statistics to compare cardiac output measurement techniques. *J Clin Monit Comput* 1999; 15:85–91
11. Lorsomradee S, Lorsomradee S, Cromheecke S, De Hert SG: Uncalibrated arterial pulse contour analysis *versus* continuous thermodilution technique: effects of alterations in arterial waveform. *J Cardiothorac Vasc Anesth* 2007; 21:636–43
12. Manecke GR: Cardiac output from the arterial catheter: Deceptively simple. *J Cardiothorac Vasc Anesth* 2007; 21:629–31

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## Muscle Relaxants and Airway Management

*To the Editor:*—The article by Schmidt *et al.* and the accompanying editorial by Boylan and Kavanagh raise a very important issue, which is the place of neuromuscular blocking drugs (NMBDs) in anesthetic practice.<sup>1,2</sup> Schmidt *et al.* state that “The use of muscle relaxants can cause severe hypoxia if the trachea cannot be intubated and the patient cannot be ventilated.”<sup>1</sup> We would be grateful if they could tell us on what evidence they base this statement. With respect, we think they may be falling into the well-known medical trap of confusing subsequence with consequence.<sup>3</sup> In our opinion a more realistic and up-to-date statement would be “If mask ventilation is impossible, the evidence suggests that an NMBD will permit ventilation or intubation.”

The large study of Kheterpal *et al.* has confirmed that the nonevidence-based practice of not administering an NMBD until ventilation has been demonstrated is unsound. Of the patients in whom ventilation by face mask was impossible, all but one received an NMBD to facilitate intubation.<sup>4,5</sup> The option of waking the patient up if ventilation is impossible is often put forward as the reason for not administering an NMBD, but none of the patients with difficult or impossible mask ventilation in Kheterpal *et al.*'s study were woken up. In practice it seems that this is not an option anesthetists find expedient.

In their editorial, Drs. Boylan and Kavanagh refer to the use of NMBDs in Schmidt *et al.*'s study, writing that “The finding that their use was not associated with more complications is not surprising because they were used in the presence of the more experienced attending physicians.”<sup>2</sup> The impression given is that NMBDs are tricky substances that might cause harm to the patient if used by an inexperienced

anesthetist (in fact, Schmidt *et al.*'s study found a decrease (odds ratio [OR] 0.66) in complications associated with their use, albeit nonsignificant (95% CI 0.33–1.33), independent of any effect of the attending physician's presence).<sup>1</sup> We would like to know why Boylan and Kavanagh seem to believe that the use of NMBDs by less experienced anesthetists is hazardous. As far as we can see, the evidence shows that when NMBDs are used, mask ventilation is facilitated,<sup>6</sup> tracheal intubation is easier and less traumatic,<sup>7</sup> more successful in less experienced hands,<sup>8</sup> and facilitated when mask ventilation is impossible.<sup>5</sup> We wonder whether any of the respiratory emergency patients in Schmidt *et al.*'s study had stridor as a result of laryngo-tracheal stenosis? Nouraei *et al.* have shown that these patients achieve better gas flows than they can manage while awake if they are given an NMBD.<sup>9</sup>

Schmidt *et al.* found that opioid use was associated with an increased risk of complications and wrote that “*this is difficult to explain.*”<sup>1</sup> An obvious explanation occurs to us, which is the phenomenon of muscle rigidity associated with opioid use.<sup>10</sup> We guess that one or other of the fentanyl-type analgesics is used in the vast majority of induction regimes in the United Kingdom, and it is our experience that the timely use of an NMBD is sometimes vital. If junior anesthetists receive messages that might inhibit their use of muscle relaxants in this not uncommon situation, we, the seniors, have failed them and their patients.

We have no problem with the proposition that tracheal intubation *can* be performed in an apneic patient without the use of NMBDs. However, we are alarmed by the message that we perceive (mistakenly we hope) to be implicit in Schmidt *et al.* and Boylan and Kavanagh's