Phenylephrine Infusions for Maintaining Blood Pressure During Spinal Anesthesia for Cesarean Delivery: Finding the Shoe That Fits

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> "By three methods we may learn wisdom: first, by reflection, which is noblest; second, by imitation, which is easiest; and third by experience, which is the bitterest."
>
> —Confucius

Much has changed in the way we manage blood pressure during spinal anesthesia for cesarean delivery. There is now less reliance on IV fluid, the advent of the combined spinal–epidural technique has allowed the use of smaller intrathecal doses, and most significantly, phenylephrine has graduated from being the new kid on the block to a routine, and arguably, preferred vasopressor. Debate has now shifted from *whether* we should use phenylephrine to *how* we use it. One method that has garnered attention is the use of prophylactic infusions[1]; this has been the technique of choice in my department for more than a decade.

What are the advantages of a phenylephrine infusion? Are there disadvantages? Should it be used in routine clinical practice? What advice can be given to those wishing to adopt the technique?

Phenylephrine's primary action as an α-adrenoreceptor agonist matches the fundamental physiologic effect of sympathetic block during spinal anesthesia: vasodilation. Thus, phenylephrine is highly effective for preventing hypotension and, most importantly, the associated unpleasant maternal symptoms.[2–4] Use of phenylephrine results in higher fetal pH compared with ephedrine[5,6]; although the clinical significance of this difference is debatable, the higher pH does provide reassurance that administering phenylephrine in doses necessary to effectively prevent maternal nausea, vomiting, and dizziness is not harmful to uterine blood flow and, by extension, the fetus.

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Accepted for publication December 10, 2013.

Funding: Departmental and institutional funds only.

The author has no conflicts of interest to declare.

Reprints will not be available from the author.

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DOI: 10.1213/ANE.0000000000000111

The relatively fast onset and short duration of action of phenylephrine make administration by infusion convenient, appropriate, and effective. Parallels can be drawn with other short-acting drugs we commonly administer by infusion during anesthesia. In this issue of *Anesthesia & Analgesia*, Siddik-Sayyid et al.[7] report a randomized double-blinded study that further supports use of phenylephrine infusions. Patients having spinal anesthesia for elective cesarean delivery randomly received a prophylactic variable-rate phenylephrine infusion or saline placebo; hypotension was treated with rescue phenylephrine boluses. Consistent with previous work,[4] patients who received a phenylephrine infusion had less hypotension (20% vs 90%), less nausea/vomiting (10% vs 40%), and similar neonatal outcome compared with control. Of note, fewer physician interventions were required in the infusion group (median 0 vs 3); this is important because physicians most likely will be more willing to adopt a technique that not only improves patient outcome but also reduces their workload. The study also showed that a phenylephrine infusion resulted in greater accuracy for maintaining blood pressure near baseline compared with control (phenylephrine boluses as needed). Although extremely tight control of intraoperative blood pressure in itself is unlikely to be necessary for most patients, keeping values reasonably close to baseline probably means that potentially harmful extreme fluctuations will be less likely.

However, despite great enthusiasm by some,[1] not everyone agrees a phenylephrine infusion is the best method.[8–10] Use of intermittent boluses is simple and does not require a syringe pump. Boluses may be given as "rescue" to treat hypotension,[7] or alternatively a more proactive approach may be taken. For example, Doherty et al.[11] gave a bolus of 120 μg phenylephrine after any decrease in blood pressure below baseline; compared with patients who received a prophylactic phenylephrine infusion, there was no difference in hypotension or bradycardia. However, the total phenylephrine dose was smaller, and blood pressure was better maintained in the first 6 minutes after induction in the bolus group. These results indicate that good blood pressure control is indeed achievable with intermittent boluses. However, as the work by Siddik-Sayyid et al.[7] suggests, giving repeated manual injections is more labor intensive and, arguably, less convenient than using a syringe pump.

With large doses of phenylephrine, hypertension and maternal bradycardia can occur. Most instances should be short-lived, provided phenylephrine administration is

terminated or adjusted appropriately. Treatment of bradycardia during phenylephrine administration with anticholinergic drugs risks marked hypertension and probably should be avoided, unless there is concomitant hypotension.[12] Bradycardia results directly from a baroreceptor reflex although a decrease in venous return mediated by effects on the splanchnic circulation has also been implicated.[9] Bradycardia is of concern because a close correlation with decreased cardiac output has been demonstrated.[13,14] However, in healthy patients having elective surgery, the clinical relevance of this decrease is unknown. Although it has been suggested that correlation with uteroplacental blood flow is better with cardiac output than with blood pressure,[14,15] the evidence for this is indirect and it remains to be confirmed whether a global measure of cardiac output correlates with regional uteroplacental perfusion. Studies of phenylephrine infusions during elective cesarean delivery have consistently shown excellent neonatal outcome despite use of large doses and relatively frequent transient increases in blood pressure and decreases in heart rate, implying that these changes are well tolerated.[3,4,6,7,14,16–18] In contrast, hypotension, even of short duration, is often associated with unpleasant maternal symptoms which may impact on maternal satisfaction. Thus, although the use of large doses of phenylephrine has been criticized,[9] this technique may be acceptable if patient comfort is improved. However, when there is fetal compromise or maternal disease such as preeclampsia, more conservative administration of phenylephrine is probably prudent.

A previous editorial that promoted the use of phenylephrine infusions concluded with the recommendation "try it, you'll like it."[1] Four years later, some elaboration on this advice may be helpful. The factors that influence the incidence and severity of hypotension and vasopressor requirement, including intrathecal local anesthetic dose, baseline fluid status and fluid management, patient positioning, patient characteristics (perhaps including genetic polymorphisms), and whether the patient is in labor, will vary from institution to institution. Thus, simply imitating what one reads in a journal article may not be ideal because what works in one institution may not necessarily be appropriate in another: one shoe won't fit all. Protocols designed for the rigid conditions of a clinical trial may not be optimal for "ordinary" clinical use. For example, in several previous studies, we described a high-dose on/off algorithm for phenylephrine, the simplicity of which reduced the likelihood of protocol violations.[2–4,6,18] However, in normal clinical practice, we usually use a more flexible infusion rate.

Siddik-Sayyid et al.[7] suggested that a "variable-rate" infusion has advantages over "fixed-rate" protocols. However, there is uncertainty regarding what constitutes a fixed-rate regimen. More specifically, the infusion should be titrated to patient response: terminating or reducing the rate when the blood pressure is high and continuing or increasing the rate when the blood pressure is low. The actual thresholds for these changes will vary according to individual circumstances, and in most cases, a rigid protocol should not be necessary to achieve acceptable hemodynamic stability. Typically, the greatest hemodynamic changes occur during the first few minutes after induction of spinal anesthesia, so it is useful to start the phenylephrine infusion immediately; an initial rate of 50 μg/min, or 0.75 μg/kg/min,[7] is a good starting point. Some may also prefer to give a small bolus as an initial loading dose. Initially, blood pressure should be measured every minute and the infusion adjusted as required.

Usually, infusion rates are adjusted according to the blood pressure response; however, it is useful also to consider heart rate changes.[9] Because heart rate is measured continuously, it may provide a more sensitive or earlier indicator of hemodynamic changes, especially if noninvasive measurement of blood pressure fails, for example, because of severe shivering or apparatus cycling errors.

Ultimately, anesthesia providers should be able to develop a phenylephrine regimen based on their local experience that provides an acceptable balance between the elimination of maternal symptoms and the risks of hypertension and bradycardia. One shoe will never fit all. But with a little trial and error, most of us can eventually find something comfortable.

DISCLOSURES

Name: Warwick D. Ngan Kee, BHB, MBChB, MD, FANZCA, FHKCA, FHKAM.
Contribution: This author helped write the manuscript.
Attestation: Warwick D. Ngan Kee approved the final manuscript.
This manuscript was handled by: Cynthia A. Wong, MD.

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