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"I would have everie man write what he knowes and no more."—Montaigne

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Editorial I

Spinal anaesthesia for Caesarean delivery: keep the pressure up and don't spare the vasoconstrictors

My prediction is that within the next few years we will be treating hypotension after spinal anaesthesia in a fundamentally different way than we have during the last 20 years. We will no longer use ephedrine as the mainstay of treatment, we will be more aggressive about maintaining arterial pressure near normal, and we will worry less (if at all) about the liberal use of other vasoconstricting drugs. In another important contribution by this group, Kee and colleagues[1] provide evidence that will help us determine the optimal way for preventing the detrimental effects of maternal hypotension after induction of spinal anaesthesia for Caesarean delivery. In this study, the authors maintained maternal arterial pressure at 80%, 90% or 100% of baseline. Using umbilical artery pH as their primary outcome, they found that maintaining the arterial pressure at 100% of baseline was associated with the best outcome for the baby (highest umbilical artery pH) and the mother (less nausea).

Although it is not surprising that maintaining homeostasis is the best strategy, this study shatters the long-held notion that it is best to minimize the use of vasopressors in pregnant patients. It has long been held that vasoconstriction from predominantly alpha-adrenergic agonist drugs will decrease uterine blood flow (UBF) and be harmful to the fetus. Maintenance of low placental vascular resistance and thus better UBF was considered more important than any adverse effects resulting from a 20–30% decrease in maternal arterial pressure.

How did the notion develop that it is better to let the arterial pressure drift down rather than risk placental vasoconstriction? Several sheep studies showed that large doses of vasoconstricting drugs decreased UBF.[2 3] However, ephedrine maintained UBF much better than other pressors that are primarily vasoconstrictors and have little beta-agonist effect (e.g. phenylephrine and metaraminol). Therefore, ephedrine became the 'gold standard' for prophylaxis and treatment of spinal hypotension.

Accumulating evidence that doses of ephedrine large enough to maintain homeostasis after the induction of spinal anaesthesia may be detrimental to the fetus are causing a major change in our approach to this problem.[4] In a recent study, Cooper and colleagues[5] compared ephedrine and phenylephrine for the treatment of maternal hypotension. Consistent with other recent studies,[4] they found ephedrine caused more acidosis in the fetus. A unique aspect of Cooper and colleagues' study is their evaluation of the degree of acidosis seen in the umbilical vessels. They calculated the difference between the P_{CO_2} in the umbilical artery and umbilical vein (P_{CO_2} (art–vein)). If the P_{CO_2} (art–vein) is small, this indicates poor placental perfusion or gas exchange. For example, conditions such as placental abruption have a small P_{CO_2} (art–vein). If the P_{CO_2} (art–vein) is large, this suggests that acidosis in the umbilical artery is secondary to a process in the fetus. Cooper and colleagues found a strong correlation between ephedrine use and an increase in the P_{CO_2} (art–vein). From these data they concluded that ephedrine was stressing the fetus and may have contributed to fetal acidosis.

There is additional evidence that ephedrine may adversely affect the fetus. When ephedrine was given to women in labour, there were changes in the fetal heart rate pattern (tachycardia and abnormal increases in variability) that might indicate fetal stress or an increase in fetal metabolic activity.[6] These changes were dose related.

Other commonly used vasopressors do not have as much beta-agonist activity and thus do not increase metabolism in the fetus. For example, Cooper and colleagues[5] found no correlation between phenylephrine dose and an increase in the P_{CO_2} (art–vein). The current study, as well as others by Cooper and colleagues and Mercier and colleagues,[7] all reported use of large doses of phenylephrine given to maintain a baseline arterial pressure without any adverse effect on the fetus.

Why do these large doses of phenylephrine (sometimes over 1000 μg total dose) not cause clinically significant vasoconstriction and decreased placental perfusion? Although these large doses were needed to maintain homeostasis, they did not increase arterial pressure to supranormal levels. Therefore, these doses should be considered appropriate for correcting the vasodilatation secondary to a spinal anaesthetic.

The parturient's decreased sensitivity to sympathomimetics during pregnancy may help protect the fetus from excessive vasoconstriction. Tong and Eisenach[8] demonstrated that uterine arteries from pregnant ewes were less

responsive to vasoconstrictors compared with those from non-pregnant ewes. Giving large doses of alpha-agonists that constrict peripheral arteries and restore normal maternal arterial pressure may preferentially shunt blood to the uterine arteries, which may be relatively spared from the vasoconstrictive effect.

We must also consider the possibility that significant placental vasoconstriction does occur with phenylephrine, but may not be important with regard to fetal wellbeing. Of particular interest in Kee and colleagues' article in the current issue[1] is the trend for an increase in umbilical artery P_{O_2} to occur in conjunction with higher maternal arterial pressures (although this did not quite reach statistical significance – P=0.058). This finding is consistent with my observations during *ex utero* intrapartum therapy procedures and fetal surgery. In these cases, the fetus is at least partially extracted from the uterus but not separated from the placenta. The fetus continues to be supported by the placenta while a procedure is performed. In all instances, a pulse oximeter probe was placed on the fetus. In these cases (performed under general anaesthesia with high-dose potent inhalational anaesthetics given to provide uterine relaxation), I have observed an increase in fetal oxygen saturation of 10–20% when maternal arterial pressure was increased after administration of a vasopressor (ephedrine or phenylephrine) to the mother. Why should maintaining a higher arterial pressure increase oxygen delivery across the placenta? It may be simply that a higher perfusion pressure delivers more blood to the placenta and that this favourable effect far outweighs any variations in placental vascular diameter resulting from the doses of pressors used in recent clinical studies.

Although the current study[1] demonstrates that maintaining a higher arterial pressure increases the umbilical artery pH, is the difference of 0.02 clinically significant? Perhaps not in the healthy fetus. However, there will be cases in which compromised fetuses may benefit significantly by having maternal arterial pressure maintained and fetal oxygen delivery optimized. For example, Datta and Brown[9] showed that umbilical artery pH was only slightly decreased after Caesarean delivery in healthy mothers who experienced transient hypotension secondary to their spinal anaesthetic. However, in infants of diabetic mothers who developed similar degrees of hypotension, the umbilical artery pH decreased to a clinically significant level. Since we do not always know the adequacy of placental reserve, it makes sense to always maintain the arterial pressure near to normal values, given the data presented in Kee and colleagues' paper.[1]

While it may appear logical to assume that what constitutes good therapy for *normal* mothers and fetuses constitutes good therapy for the compromised maternal–fetal unit, this may not always be the case. In reality, we do not really know how findings in normal subjects transfer to unhealthy mothers or fetuses. For example, what is the optimal maternal arterial pressure for a pre-eclamptic patient? In a recent study, Dyer and colleagues[10] found that among patients with severe pre-eclampsia, the outcome for the baby was better if the mother had a general anaesthetic rather than a spinal anaesthetic. The spinal anaesthetic group received more ephedrine and presumably suffered from a greater incidence of hypotension compared with the general anaesthetic group. Would the outcome have favoured spinal anaesthesia had that group's arterial pressure been managed more aggressively with phenylephrine? The paper by Kee and colleagues[1] does not answer this question, but important studies usually create more questions than they answer. Numerous studies have now demonstrated the superiority of phenylephrine for management of spinal hypotension in healthy mothers and babies. We now need more studies on the effects of hypotension and vasoconstrictors in situations of maternal or fetal compromise.

Although there is much more to learn about hypotension and spinal anaesthesia for Caesarean delivery, we already have a wealth of information to help guide therapy. How should we prevent and treat the hypotension associated with spinal anaesthesia? The following are my recommendations:

Leg wrapping. A recent meta-analysis[11] showed that wrapping the legs with elastic bandages or the use of thromboembolic stockings prevents hypotension.

Colloid preload. The same meta-analysis[11] found that colloid preloads prevented hypotension and the individual studies found improvements in outcome measures such as Apgar scores, ephedrine use, lower maternal heart rate, less nausea and less severe hypotension.[12–14] Crystalloid preloads are largely ineffective.

Eliminate or drastically limit the use of ephedrine. Every study that has compared ephedrine and phenylephrine has found more acidosis in the fetus when the mother was given ephedrine.[4] Although it makes theoretical sense to restore both beta- and alpha-adrenergic tone after the induction of a high sympathectomy from spinal anaesthesia, limit the use of ephedrine. For anaesthetists who are concerned with the possible bradycardia associated with a high spinal or the reflex bradycardia associated with the use of vasoconstricting drugs such as phenylephrine, the use of a mixture of ephedrine and phenylephrine will keep the heart rate up and the dose of ephedrine low enough not to be detrimental to the fetus.[7]

Treat the hypotension aggressively. To reiterate what I said earlier, the use of ephedrine leads to acidosis in the fetus. The aggressive use of phenylephrine and other pure alpha-vasoconstrictors is apparently the best practice. At least, that is what the data provided by Kee and colleagues suggest.

The data in the literature support the above practices. Now what are needed are studies that evaluate how these changes in management affect outcomes. With the new management strategies, will the umbilical artery pH in babies delivered to mothers having spinal anaesthesia be as good as the values of the mothers having epidural or general

anaesthesia? Can we decrease adverse neurological outcomes? Will there be fewer neonatal intubations or admissions to the neonatal intensive care units? Are these the optimal strategies for the compromised maternal–fetal unit? Hopefully, Kee and colleagues will continue their excellent work and help us answer some of these questions.

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