such data are available, do not "throw away" the ephedrine syringe, but rather use a common sense approach based on sound clinical judgment when treating maternal hypotension in this setting.

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References


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In Reply:

I thank Drs. Kempen, Gambling, and McLaughlin for their interest and comments concerning the articles by Ngan Kee et al.1 and Dyer et al.2 regarding phenylephrine infusions during spinal anesthesia for cesarean section and my editorial3 about the relative lack of acceptance of phenylephrine, especially as an infusion, for the treatment or prevention of hypotension and other side effects in that clinical context.

Dr. Kempen provides a detailed and interesting discussion of the clinical and research protocol followed by the Ngan Kee group and raises possible alternative pharmacokinetic explanations for some of the findings. Many of these points were raised in the review process (of which I was a part), including issues concerning the dosing strategy and the determination of the "baseline blood pressure" in the operating room, as opposed to preoperatively as is perhaps more usual in studies of this kind. On balance, the other reviewers and I believed that the information obtained from the study far outweighed any limitations. Dr. Kempen refers to the dosing strategy in the study by Ngan Kee et al. as "high-dose vaspressor therapy for ASA1–2 [American Society of Anesthesiologists physical status 1 and 2 [patients]]," suggesting that these healthy women were overtreated or unnecessarily treated to prevent hypotension. I had discussed this type of objection to phenylephrine infusions; basically that this is usually not a "life and death issue" and that the clinical differences compared with older, perhaps simpler, therapies (e.g., bolus ephedrine) are small.3 The thrust of my opinion was that I disagree with this view; obstetric anesthesiologists have been searching for a solution to the spinal hypotension problem for decades (hence the "Holy Grail" metaphor), and it is notable that when a reasonable solution appears within grasp, fewer clinicians than expected are using it or are even aware of the evidence for its safe use. Dr. Kempen states that there was an increased incidence of hypertension in the phen-
phenylephrine group (47% vs. 41%), but he has apparently misread the lines in table 4; the incidences are not different ($P = 0.55$), rather it is the maximum-recorded systolic pressures that are slightly different, and probably not truly statistically so, given the multiple comparisons made (139 vs. 134 mmHg, $P = 0.044$). He also suggests that the one neonate with an Apgar score of less than 7 (it was 6), whose mother had been randomized to the phenylephrine group, may be a “subtle warning.” This suggestion based on one subject is hard to take seriously. The issue of whether to assess and treat patients based on systolic blood pressure or based on mean blood pressure is a valid point. The differential effects of vasopressor on the systolic, mean, and diastolic blood pressure is a subject that has not received enough attention.4 Right or wrong, however, the majority of anesthesiologists use the systolic blood pressure as their treatment target during cesarean delivery, and almost all previous studies have treated this based on the systolic blood pressure. Dr. Kempen also suggests that bolus dosing is less likely to result in “over-infusion,” by which he presumably means an increased incidence or severity of hypertension or perhaps bradycardia; this point is similar to that raised by Gambling. My editorial comments were not meant to recommend any particular dosing strategy for phenylephrine infusion, and specific protocols used in research studies may not always be the proper ones to use in general clinical practice,5 but the evidence is clear from multiple studies that phenylephrine infusions lead to a better control of blood pressure and a significant decrease in maternal side effects compared with ephedrine.6–9 In my personal practice, I tend to use a somewhat more moderate dosing strategy than that used by the Ngan Kee group, starting at 50 µg/min and titrating up to 100 µg/min or down to 25 µg/min or 0 µg/min each minute based on systolic blood pressure. A 100-µg/min on/off strategy used by Ngan Kee et al.10,11 has the undeniable advantage of simplicity.

Dr. Gambling’s comments are easier for me to address. I have the highest respect for his knowledge and judgment in the field of obstetric anesthesia because he has been in the forefront of research and practice for more than two decades, with early or groundbreaking work in several areas of clinical obstetric anesthesia.12–14 Thus, I am pleased that his and Dr. McLaughlin’s comments do not really contradict or refute any of the points I tried to raise in my editorial; in fact, I essentially agree with all of their statements. Certainly, phenylephrine is not always effective and can cause bradycardia-rhythms (although I am not as sure that infusions are more likely to cause this), and the clinical importance of the small but consistent difference in acid–base status reported with phenylephrine is far from clear. However, in the absence of other evidence, it would be hard to argue that a drug (ephedrine) that results in a lower neonatal pH is preferable. The issue of whether Apgar scores or umbilical cord gases are the issue to discuss, although at least one study has reported better Apgar scores with phenylephrine versus ephedrine.7 In studies of healthy women undergoing elective cesarean sec-

References


We thank the correspondents for their interest in our article.1 A

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number of points were raised, which we shall address in turn. Dr. Kempen describes our methodology as “questionable”

Dr. Kempen criticizes us for deviating from the so-called “standard” or “typical” care and methods. For example, he

points out that our protocol (similar to our usual clinical practice) did not include the use of intravenous prehydration or routine supplemental oxygen. We make no excuse for this because we consider these practices are supported by little scientific evidence.7–10

Just because something has been done for a long time does not mean it is right. Dr. Kempen stated that we provided no indication of the number of patients given oxygen, but careful reading of our article reveals this information in the final sentence of the results.

We titrated vasopressors to maintain maternal blood pressure near to baseline values. Our estimations of the latter were indeed derived from “on the table” initial recordings after arrival in the operating room. We acknowledge that this may not be ideal, but we were careful to make multiple measurements, continued this until a degree of stability was achieved, and then averaged three recordings. Dr. Kempen suggests that it may have been better to rely on clinical outpatient measurements, but one might levy equal criticism at what would likely be single measurements using different equipment taken in nonstandardized hospital conditions. In addition, Dr. Kempen states that Chinese exhibit lower pressures than Americans but provides no reference for this. The calculated mean baseline systolic blood pressure for patients in our study was 114 mmHg (SD, 9.9 mmHg). We would not regard this as being particularly low (from being Chinese) or high (from being anxious).

We agree that oscillometric measurement of blood pressure is prone to motion artifact, but we persist in using this method because it remains the most common method in clinical practice. We agree that mean arterial pressure may be a better indicator of perfusion pressure, but nevertheless, systolic pressure remains a clinically useful endpoint on which to base therapy,11 and many clinicians and researchers continue to use it. Interestingly, Dr. Kempen refers to measurement of blood pressure in “Torr.” Our equipment is calibrated in millimeters of mercury, which numerically is close to “Torr” but is not exactly equivalent.*

Dr. Kempen states incorrectly that we “simply stopped” the infusion if systolic blood pressure was greater than base-