Possible Influence of Decreasing Maternal Ephedrine Requirements on Fetal/Maternal Concentration Ratio at Delivery

To the Editor:

I read with great interest the article by Ngan Kee et al.1 It makes a significant contribution to our understanding of the fetal effects of ephedrine during spinal anesthesia for cesarean section. Placental transfer was found to be considerably greater for ephedrine than for phenylephrine, as evidenced by a markedly higher umbilical vein to maternal artery ratio with ephedrine. Interestingly, the umbilical vein to maternal artery ratio was greater than unity for ephedrine, which the authors suggest may have been caused by ion trapping. Could another factor have contributed to this (and to the magnitude of the difference between the groups)? The samples were taken at one point in time (delivery) during a dynamic situation. Ephedrine has a slower onset and a longer duration of action than phenylephrine. During spinal anesthesia for cesarean section, we have observed that ephedrine requirements decrease more rapidly over time than phenylephrine requirements.2 During the second 15 min after spinal anesthesia, we observed ephedrine requirements to be 26% of those in the first 15 min compared with 79% for phenylephrine. If maternal ephedrine concentration was decreasing before delivery, this may have decreased, or even caused a reversal in, the maternal/fetal concentration gradient for ephedrine at the time of delivery.

David W. Cooper, M.B.B.S., F.R.C.A., James Cook University Hospital, Middlesbrough, Cleveland, United Kingdom. drdavidcooper@aol.com

References


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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. and Dyer et al. regarding phenylephrine infusions during spinal anesthesia for cesarean section and my editorial 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. 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 vasopressor 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. 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 phenolephrine infusion group compared with the ephedrine group.

Table 1. Umbilical Artery pH and Base Excess from Two Studies Comparing Ephedrine and Phenylephrine for the Treatment of Hypotension during Cesarean Delivery with Spinal Anesthesia

<table>
<thead>
<tr>
<th>Phenylephrine</th>
<th>Ephedrine</th>
<th>Parameter Measured</th>
<th>P Value</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>7.33 (7.30–7.35)</td>
<td>7.25 (7.14–7.29)</td>
<td>µA pH</td>
<td>&lt; 0.001</td>
<td>1</td>
</tr>
<tr>
<td>−1.9</td>
<td>−4.8</td>
<td>Base excess</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>7.31</td>
<td>7.28</td>
<td>µA pH</td>
<td>NS</td>
<td>2</td>
</tr>
<tr>
<td>−1.34</td>
<td>−4.75</td>
<td>Base excess</td>
<td>2</td>
<td></td>
</tr>
</tbody>
</table>

The values are given as mean (range). NS = not significant.

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.

David R. Gambling, M.B., B.S., F.R.C.P.C.,* Kimberly Robbins McLaughlin, M.D. *Sharp Mary Birch Hospital for Women and Newborns, San Diego, California, and University of California, San Diego, San Diego, California. david.gambling@sharp.com

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Correspondence

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