LETTER TO THE EDITOR

Phenylephrine Versus Ephedrine for the Management of Hypotension in the Obstetric Patient; Do We Have an Updated Answer?

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Lin et al. [1] performed an updated meta-analysis of the use of ephedrine versus phenylephrine for the management of hypotension associated with spinal anesthesia for cesarean delivery. The authors concluded that there was no difference in efficacy between the two agents when used for the prophylaxis or treatment of hypotension and that phenylephrine use was associated with higher umbilical artery and vein pH compared with ephedrine when used for the treatment of established hypotension, but not when given prophylactically. However, I am concerned about several methodological issues in the synthesis of the presented results. In particular, the authors grouped all trials comparing the two vasopressors with no consideration to the regimen used, dose, or potency ratio of phenylephrine versus ephedrine, which undoubtedly have an impact on outcomes. For instance, the studies by Alahuhta et al. [2], Cooper et al. [3], and Hall et al. [4] used phenylephrine infusion regimens of 10–33 $\mu\text{g}/\text{min}$ and an ephedrine infusion regimen of 0.8–2 mg/min , while Ngan Kee et al. [5] used infusion rates of 100 $\mu\text{g}/\text{min}$ and 8 mg/min of phenylephrine and ephedrine, respectively. This big difference in dosages affects outcomes and likely contributes to the significant heterogeneity seen in the analysis for hypotension following prophylactic intravenous vasopressor administration, and therefore, the appropriateness of pooling those studies is questionable. Different regimens were also pooled together again adding to the heterogeneity; for instance, Magalhaes [6] used a prophylactic bolus of 10 mg ephedrine or 80 μg phenylephrine followed by further boluses for the treatment of hypotension, which is very different from the regimens using a continuous prophylactic infusion as in the studies by Cooper et al. and Ngan Kee et al. [3,5]. Furthermore, some key stud-

ies were not included in this meta-analysis; for instance, a study by Ngan Kee et al. [7] reporting a significantly lower incidence of hypotension following prophylactic infusion of phenylephrine compared with ephedrine was not included in the efficacy analysis, and several studies reporting on umbilical arterial and venous pH following prophylactic use of the two vasopressors, with most reporting higher pH with phenylephrine, were also not included in the pH analyses [3,5,7,8]. If those results were reported in formats other than mean and standard deviation, an attempt to contact the authors of the original articles or transform the data to the appropriate format could have been performed, instead of simply omitting those data from the analysis. The report also lacks a display of the results of individual studies on the forest plots, therefore limiting the ability of the reader to assess what the authors have performed. For the treatment studies, it is not clear what the incidence of hypotension refers to; does it refer to recurrent hypotension after administration of the vasopressor? A number of endpoints relevant to this meta-analysis could have been included such as base excess, Apgar scores, and the incidence of bradycardia, reactive hypertension, and intraoperative nausea and vomiting.

In summary, while this meta-analysis addresses a topic of significant interest to the obstetric anesthesiologist [9], methodological shortcomings, questionable appropriateness of pooling trials, and lack of inclusion of relevant studies cast some doubt on the conclusions reached by the authors.

Conflict of Interest

The author declares no conflict of interest.

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