Determinition of the ED90 of Metaraminol to Avoid Hypotension After Spinal Anesthesia for Elective Cesarean Delivery

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Background: Phenylephrine has become the vasopressor of choice to prevent/treat hypotension during cesarean delivery (CD) under spinal anesthesia; however, its use may induce bradycardia and decrease cardiac output. Metaraminol is less likely to induce bradycardia and may be advantageous. Metaraminol has been shown to be superior to phenylephrine when used in a continuous infusion (1), but there is no published dose-response study on metaraminol used as an intermittent bolus in CD.

Methods: After IRB approval and informed consent, term pregnant women undergoing elective CD under spinal anesthesia were recruited into this double-blinded study. Following standard spinal anesthesia (hyperbaric bupivacaine 0.5% 12.5mg, fentanyl 25µg and morphine 100µg), SBP and HR were assessed every minute until delivery, and a bolus dose of metaraminol was given whenever the SBP was < baseline. An adequate response was defined as the absence of hypotension (SBP<80% baseline) before delivery. The metaraminol dose was determined as per a biased coin up-down sequential allocation scheme to estimate the 90% effective dose (ED90). The initial dose was 25µg, and it was adjusted by 25µg increments or decrements in the subsequent patients. The stopping rule used was the development of hypertension (SBP>20% baseline), or the inclusion of 50 patients. In cases of treatment failure, a standard rescue dose of metaraminol 250µg was used. The linearly interpolated ED90 estimator was calculated using Pool-Adjacent-Violators Algorithm (PAVA) isotonic regression, and 95% confidence intervals (CIs) were estimated using a parametric bootstrap routine (2).

Results: Forty-eight women were approached to participate, and 43 consented. The highest dose used was 325µg. The ED90 of metaraminol was estimated at 314µg (95% CI, 282-321µg). The response of each subject to the treatment is shown in the figure. Two patients presented with bradycardia with doses of 150µg and 275µg. Only the last patient of the study exhibited hypertension (325µg).

Discussion: This is the first dose-response study of metaraminol used in bolus doses in CD, and the ED90 is 314µg. The incidence of hypertension is much lower than that reported in a similar study with phenylephrine (3), and these Results are encouraging. Further trials making a direct comparison between phenylephrine and metaraminol are warranted.
