

Title: EPHEDRINE SULFATE AS THE INTRAVENOUS COMPONENT OF THE EPIDURAL ANALGESIA TEST DOSE IN LABORING PARTURIENTS

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Introduction. The efficacy and safety of epinephrine as the intravenous component of the epidural test dose in obstetrical patients has been questioned. (1) Therefore, ephedrine sulfate, the vasopressor of choice in parturients, was evaluated as a possible alternate.

Methods. Approval from the institution's Human Rights Committee and participant informed consent was obtained. We studied 45 normotensive ASA class I or II full term parturients, receiving lumbar epidural analgesia (LEA) for labor, without signs of fetal distress. Parturients were supine with left lateral uterine displacement, except where noted below, and prehydrated with 1 liter Ringer's lactate. Maternal heart rate (HR) was determined by electrocardiogram and palpation and blood pressure (BP) by auscultation of Korotkoff sounds. Uterine contractions and fetal HR were continuously monitored electronically. Maternal HR and BP were measured with and without contractions and after positioning the parturient for induction of LEA in either the sitting or lateral decubitus position. A lumbar epidural catheter was inserted. Simultaneously, as the epidural catheter was flushed with 3 ml normal saline (NS), the parturient randomly received the "test dose" of either 3 ml NS or 3 ml NS with 15 mg ephedrine sulfate intravenously (iv). The parturient's HR and BP were monitored immediately after this iv injection and every minute for 10 min and finally every 3 min for 15 min in the absence of contractions. Beginning 5 minutes after the iv injection, the parturient received slow incremental doses of 0.25% bupivacaine epidurally to achieve a tenth thoracic dermatome level of sensory blockade to pin prick.

Prior to each reinforcement of LEA, the parturient's baseline HR and BP were obtained with and without contractions. She then received either 3 ml NS or 3 ml NS with 15 mg ephedrine sulfate intravenously. HR and BP measurements were taken according to the above protocol. Five minutes after this iv injection, LEA was reinforced as before to a tenth thoracic dermatome level of sensory blockade.

The same investigator, blinded to "test dose" contents, took all of the measurements for any individual reinforcement and was asked to "guess" which had been administered. Apgar scores and the mode of delivery were noted in all participants. The maximum maternal systolic and diastolic BP and HR occurring within 5 minutes after the iv "test dose" injection were analyzed. BP and HR data are reported as mean \pm 1 S.D. and were analyzed using the paired t-test with Bonferroni inequality. Apgar scores, mode of delivery and the "blinded" investigator's subjective assessment of the intravenous "test dose" contents were analyzed using chi-square analysis with Yates' correction or the Fisher exact test as needed. $P < 0.05$ was considered statistically significant.

Results. The parturients' mean maximum systolic blood pressures were:

- 124.1 \pm 14.6 mmHg without contractions
- 131.6 \pm 16.5 mm Hg with contractions
- 132.7 \pm 12.6 mm Hg in the sitting position
- 121.0 \pm 16.8 mm Hg in the side position

- 130.1 \pm 15.5 mm Hg after 3 ml NS iv
 - 146.6 \pm 20.9 mm Hg after 15 mg ephedrine sulfate iv
- $P < 0.05$ for the comparisons of a-e, a-f, b-f, c-f, and d-f.

The mean time to peak systolic BP after the iv "test dose" was 2.2 ± 1.1 min. The "test dose" containing 15 mg ephedrine sulfate produced statistically significant increases in maximum maternal systolic BP above those seen prior to the induction of LEA without contractions, with contractions and with positioning. Maximum maternal systolic BP after iv ephedrine sulfate increased 18.7 ± 13.3 % over maternal systolic BP without contractions and 12.4 ± 10.8 % above maternal systolic BP with contractions. The "blinded" investigator prediction of which iv "test dose" had been given was correct 72% of the time.

Despite statistical significance in the maximum maternal diastolic BP and HR data, these percentage increases were lower than the increases seen in the maximum maternal systolic BP. Regardless of the "test dose" substance, there was no difference in Apgar scores or the incidence of vaginal delivery versus cesarean section. Of note is that after receiving ephedrine sulfate some patients developed a transient fetal tachycardia (>160 beats/min) that required no medical intervention.

Discussion. To be effective the iv component of the epidural test dose in laboring parturients must safely and rapidly signal an inadvertent iv injection with a maternal reaction that is clearly discernable from the normal hemodynamic changes that occur secondary to the stresses of labor. Epinephrine, 15 mcg, which was widely used as the iv component of the epidural test dose has been shown to cause a brief maternal tachycardia of ≥ 10 beats/min which may be followed by maternal bradycardia and fetal distress. (1) Therefore, ephedrine sulfate, which unlike epinephrine does not cause a decrease in uteroplacental blood flow, was evaluated as the possible iv component for the epidural test dose. (2) Our results show that, unlike the group receiving NS alone, there was a statistically significant increase in the maximum maternal systolic BP after 15 mg iv ephedrine sulfate above those seen with all of the normal stresses of labor. However, because of the large interpersonal variability (ie. large standard deviation), the predictions by the "blinded" investigator were incorrect in 28% of the cases. Therefore, in spite of the statistical significance, 15 mg ephedrine sulfate would be a clinically unreliable iv component of the epidural test dose in laboring obstetrical patients.

References.

- Leighton BL, Norris NC, Sosis M, Epstein R, Larijani GE: Limitations of an epinephrine epidural anesthesia test dose in laboring patients. *Anesthesiology* 65:A403, 1986
- Hollmen AI, Jouppila R, Albright GA, Jouppila P, Vierola H, Koivula A: Intervillous blood flow during caesarean section with prophylactic ephedrine and epidural anaesthesia. *Acta. Anaes. Scand.* 28:396-400, 1984