Title: EFFECTS OF EPHEDRINE AND PHENYLEPHRINE ON PULMONARY ARTERIAL PRESSURE IN PATIENTS WITH CERVICAL, LUMBAR EPIDURAL OR ENFLURANE ANESTHESIA

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Introduction. Almost 30 years ago, Aviado[1] reviewed the cardiovascular effects of 26 pressor agents including ephedrine and phenylephrine used in clinical practice and pointed out that no definitive information regarding their effects on pulmonary circulation existed in humans. Since then the pulmonary circulation has been shown to differ from the systemic circulation with respect to its autonomic regulation[2,3].

Ephedrine (EP) and phenylephrine (PH) are old but still commonly used in modern clinical anesthesia. Their systemic cardiovascular actions are well-documented, however their actions onto the pulmonary circulation in humans are not confirmed and can only be predicted by pressor agent' pharmacological properties. Therefore, we studied the effects of EP and PH on pulmonary circulation in humans anesthetized with either cervical or lumbar epidural anesthesia, or neither.

Methods. Fifty two adult patients (44 males and 8 females, 35-80 yrs of age) scheduled to undergo elective surgeries and indicated to have both arterial and pulmonary arterial lines in place during anesthesia were studied. The protocol has been approved by our local review committee. The anesthetic techniques were as follows; cervical epidural + N_2O, O_2 (n=19), lumbar epidural + N_2O, O_2 (n=17), enflurane + N_2O, O_2 (n=16). Before the initiation of surgical procedures when AP decreased to or below 80% of the resting awake value, intravenous bolus of either EP (0.2±0.05 mg/kg) or PH (25±8 μg/kg) was performed. The following variables were either recorded continuonsly or measured intermittently prior to or following the administration of the agents: arterial pressure (AP), heart rate, central venous pressure, pulmonary arterial pressure (PAP), pulmonary arterial occlusion pressure (PAOP) and cardiac output (CO). For statistical analyses, ANOVA and student's t test were used. P. values less than 0.05 were considered to indicate statistically significant difference.

Results. Both EP (0.2±0.05 $mg.kg^{-1}$) and PH (25±8 $\mu g.kg^{-1}$) produced a significant increase in pulmonary arterial pressure (PAP) with concomitant increase in arterial pressure (AP). In the patients with cervical epidural block and N_2O-O_2, systolic PAP increased 22±5 to 28±8 mmHg with EP and 23±6 to 32±10 mmHg with PH in response to approximately 30 mmHg increase of AP, and the ratio of the increment of systolic PAP to systolic AP (ΔPAP/ΔAP) were 0.15±0.08 with EP and 0.20±0.13 for PH ($p<0.05$); these did not differ significantly from the changes observed in the patients having lumbar epidural, but differed in those with enflurane-N_2O-O_2 (table 1). The influence on cardiac output (CO) differed significantly between EP and PH; EP increased CO significantly in the three anesthetic groups, while PH did not elicit any significant changes of CO. There was a significant relationship between ΔPAP and ΔAP elicited by EP or PH in all patients studied; a regression equation was ΔPAP=0.22xΔAP-2.9 for EP (r=0.77) and ΔPAP=0.11xΔAP+4.1 for PH (r=0.38).

Discussion and Conclusion. Our data are indicative of differential pulmonary hypertensive mechanisms by EP from PH. PH mainly acts on the pulmonary vasculature possibly via its α-adrenergic action thereby vascular constriction plays a major role. On the other hand EP-induced increase in CO could contribute to the increase in PAP as suggested by Aviado[1]. Although the PAP effects of EP and PH differed significantly, 1.4 and 1.9 mmHg increase per a 10 mmHg increase in AP, respectively, either effect may not be significant clinically in patients without cardiovascular complications. Since we found no differences in the responses of PAP to either agent between patients with and without cardio-pulmonary sympathetic denervation induced by epidural block, it is assumed that preexisting pulmonary vascular tone is unlikely to be an important factor determining the PAP responses. Rather the PAP responses to either agent appear to differ in individual patients with different pulmonary vascular reactivity.

References.
1. Aviado DM: Cardiovascular effects of some commonly used pressor amines. Anesthesiology 20:71-97, 1959
2. Hyman AL, Lippton HL, Kadowitz PJ: Autonomic regulation of the pulmonary circulation. J. Cardiovas. Pharmacol. 7:S80-S95, 1985
3. Hyman AL, Kadowitz PJ: Enhancement of α- and β-adrenoceptor responses by elevations in vascular tone in pulmonary circulation. Am. J. Physiol. 250:H1109-H1116, 1986

Table 1. Number of Patients (M/F) for six groups, and PaO_2, $PaCO_2$, and ΔPAP/ΔAP to EP or PH.

Anesthetic Techniques	Drugs	M/F (44/8)	During Anesthesia PaO_2 (mmHg)	$PaCO_2$ (mmHg)	ΔPAP/ΔAP
Cervical Epi. + N_2O, O_2	EP	7/2	167±36	41±5	0.15±0.08
	PH	9/1	159±37	39±4	0.20±0.13
Lumbar Epi. + N_2O, O_2	EP	8/1	169±24	35±4	0.16±0.09
	PH	8/0	169±13	35±5	0.20±0.13
Enflurane + N_2O, O_2	EP	5/3	149±30	36±6	0.17±0.08
	PH	7/1	157±33	37±2	0.17±0.07