

Title: DIABETES INDUCED SENSITIVITY OF AORTIC CONTRACTION TO PHENYLEPHRINE IS TIME AND ENDOTHELIUM DEPENDENT

Authors: K.S.K. Chang, M.D., W.G. Stevens, M.D. and M.O. Lacy

Affiliation: Depart. of Anesth., Oregon Health Sciences Univ., Portland, OR 97201

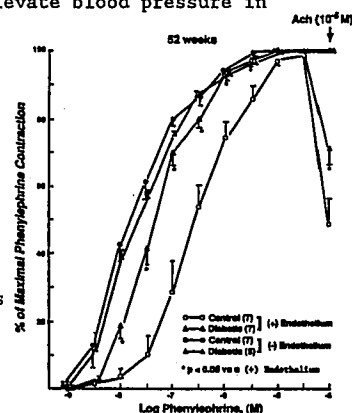
Introduction. Hypertension (HT) frequently accompanies diabetes mellitus (DM). If DM enhances vascular responsiveness to alpha-adrenergic stimulus(1), hypertension would be abetted. To test whether the vascular response is related to duration of DM and whether damage of the endothelium plays a role in the changes of the response, we measured the vascular responses to phenylephrine (PE) in the isolated rings of aorta with and without endothelium (ED) from male Sprague-Dawley rats made diabetic (D) with streptozotocin (55 mg/kg, IV) and controls. **Methods** Twelve and 52 weeks after induction of diabetes, thoracic aorta of D and age matched C rats were removed, cut into rings (3 mm width). Each ring was suspended in an organ bath in Krebs-Henseleit solution (37°C), aerated with 95% O₂/5% CO₂ and their contraction recorded isometrically under 2 gm tension. Cumulative concentration response curves of PE were obtained prior to and after removal of ED. After obtaining maximal contraction of PE, acetylcholine (Ach) 10⁻⁵M was added to the bath to induce relaxation. PE responses were expressed as mg of developed tension/mg of aortic tissue and

also percent of maximum PE contraction. **Results.** When ED was present, D rats demonstrated increased sensitivity to PE at 52 weeks but not at 12 weeks. When ED was removed, there were no differences in PE sensitivity between C and D rats. Ach induced relaxation, which is ED dependent(2), was significantly less in the 52 wk diabetic aorta with intact ED. **Discussion.** Our results indicate DM significantly increases PE sensitivity in long term DM and damage of ED may play a role in the increased sensitivity to PE and lead to development of hypertension in DM. If a similar effect occurs in man, smaller amounts of alpha-adrenergic stimulant may be required to elevate blood pressure in diabetic patients.

References

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A560

TITLE: EFFECTS OF PROPOFOL ON THE CONTRACTILE STATE OF ISOLATED RABBIT PAPILLARY MUSCLES UNDER VARIOUS STIMULATION CONDITIONS

AUTHORS: B.F. Rusy, M.D., P.Y. Thomas-King, M.D., G.P. King, M.D., H. Komai, Ph.D.

AFFILIATION: Department of Anesthesiology, University of Wisconsin, Madison, WI 53792

Propofol causes depression of cardiac contractility in vivo.¹ Little is known concerning its direct inotropic effects in isolated ventricular tissue.^{2,3} We have examined the actions of propofol on rested state, steady state, and potentiated state contractions in rabbit papillary muscles in order to determine the relative importance of its effects on the transsarcolemmal influx and the internal sarcoplasmic reticular (SR) release of activator calcium.

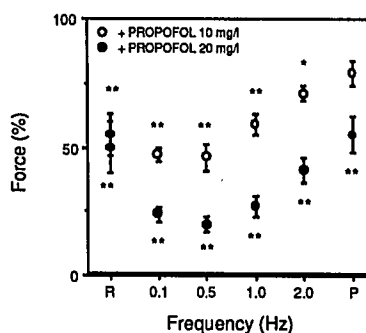
Following Institutional approval, papillary muscles (n = 6) isolated from the right ventricles of pentobarbital-anesthetized rabbits were superfused with a Krebs-Henseleit medium at 30°C. The muscles were field stimulated electrically to cause rested state (contraction after 20 min rest), steady state (0.1 to 2.0 Hz), and potentiated state (post-rest) contractions. Dunnett's t-test was used to evaluate the effect of propofol vs control, p < 0.05 being considered significant.

Addition of propofol (10, 20 mg/l) caused significant depression of the contractile force of rested state and steady state contractions with the greatest effect at 0.1 and 0.5 Hz. Post-rest potentiated state contractions were significantly inhibited only by the higher concentration of propofol (Figure).

Rested state contractions in rabbit ventricular tissue are known to be activated primarily by activator calcium which is derived transsarcolemmally⁴ while potentiated state contractions are activated by calcium released internally from the SR.⁵ These results suggest

that propofol, in concentrations likely to be encountered clinically,⁶ has a significant negative inotropic effect which is caused via depression of both sarcolemmal and SR function, the former being most affected. Research supported in part by NIH GM 29527.

Fig. Mean ± SEM (n = 6). *p < 0.05, **p < 0.01, compared to control.



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