TITLE: VASOACTIVE ACTIONS OF BUPIVACAINE AND 2-CHLOROPROCAINE ON UMBILICAL VASCULAR SMOOTH MUSCLE

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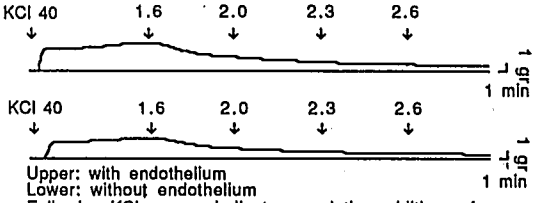
The importance of vascular endothelium in smooth muscle responsiveness has recently been discovered. Many vasoactive agents exert their action via release of endothelium-derived vasoactive factors. The release of endothelium-derived relaxing factor (EDRF) from umbilical vessels has been suggested, although its action on umbilical smooth muscle is not known. Studies have demonstrated that many substances, including local anesthetics, are vasoactive on umbilical vessels. The present study concentrates on the role of the endothelium in umbilical vascular reactivity, with emphasis on the vasoactive mechanism of the local anesthetics.

Umbilical arteries and veins were prepared as paired rings. One member of each pair was treated to remove the endothelium, while the other member served as a control. Endothelium removal was accomplished by either mechanical rubbing of the intima or exposure for 15 minutes to 1, 20, or 100 µg/ml of saponin, a detergent reported to cause endothelium removal. Isometric tension recordings to three known contractile agonists (histamine, 2.7 x 10-4M, 5-hydroxytryptamine, 2.5 x 10-7M, and potassium chloride, 8 x 10-2M) and to two local anesthetics (bupivacaine, 2.2 x 10-5M - .3 x 10-4M, and 2-chloroprocaine, 1.6 x 10-4M-2.6 x 10-3M) were studied. Responses were quantitated for treated and untreated preparations, and compared by paired t test. Repeated histologic study confirmed preparation integrity. Responses to the agonists, and to the local anesthetics, in rubbed vessel rings did not differ from control (Figure). Known agonist-induced contractions in saponin-treated vessels trended toward lower tension development as compared to control, although significance was not consistently seen. Intimal rubbing was effective in removing 70 - 100% of the endothelium. However, saponin at the concentrations and duration used was not effective in endothelial cell removal.

This study shows that: 1) for endothelium removal, intimal rubbing is superior to saponin treatment; 2) in vitro umbilical vessel preparations retain normal appearing morphology and cellular integrity, as defined by high power light microscopy; 3) the relaxation caused by 2-chloroprocaine, as shown in previous studies, is not endothelium-dependent; 4) similarly, bupivacaine-induced contraction is not altered by the presence or absence of endothelium.

Response of Umbilical Venous Ring to 2-Chloroprocaine Following KCl-Induced Submaximal Contraction



Upper: with endothelium
Lower: without endothelium
Following KCl, arrows indicate cumulative additions of 2-chloroprocaine
Concentrations are expressed as 10-3M

TITLE: TRIFLUOROACETYLATED PROTEINS IN LIVERS OF RATS TREATED WITH THE POTENTIAL CHLOROFLUOROCARBON REPLACEMENT (1,1,1,TRIFLUORO-2,2-DICHLOROETHANE) (HCFC-123)

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As a result of ozone depletion by chlorofluorocarbons (CFCs) the elimination of these compounds has been proposed and replacements are being sought (1-3). The addition of hydrogen atoms to CFC molecules should allow substantial degradation of these compounds in the lower atmosphere, with little depletion of stratospheric ozone. HCFC-123 is a compound currently under investigation as a CFC replacement. Because of its structural similarity with halothane (1,1,1,-trifluoro-2-bromo-2-chloroethane), we investigated the metabolism of HCFC-123 in male Fischer 344 rats.

Rats were placed in inhalation chambers. Group 1 received air for 2 hours, group 2, 1.3% halothane for 2 hours, while groups 3 and 4 received 1.1% and 0.7% HCFC-123, respectively, for 2 hours. All rats were killed 15 hours post-exposure and liver microsomal and cytosol fractions were prepared. Following SDS-PAGE, constituent polypeptides were transferred to nitrocellulose membranes and probed with hapten specific anti-trifluoroacetyl (TFA) protein serum. Both compounds were found to produce identical patterns of TFA labeling of proteins by immunoblotting.

Halothane hepatitis has all the signs of a drug-induced hypersensitivity response (4). The finding that HCFC-123 also leads to the formation of TFA labeled proteins raises the possibility that susceptible individuals repeatedly exposed to this agent may become sensitized and develop hepatitis. It is also possible that individuals sensitized to HCFC-123 might be at increased risk for hepatic damage following anesthesia with halothane, or enflurane which can cross react with halothane (5). These results underscore the need for further metabolic and toxicologic studies before widespread introduction of HCFC-123.

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